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ABSTRACT

During this 3-day workshop with 138 registered participants, invited medical experts deliberated extensively on the physiological regulation of blood pressure, the unique biological characteristics and dietary patterns of Blacks and other minorities, the prevalence of hypertension in U.S. Blacks and Native Americans, the roles of specific macro- and micro-nutrients in the genesis of obesity and high blood pressure, and the childhood antecedents of high blood pressure in adult life. This publication presents the 17 papers given at the workshop and discussions of the papers. (JD)

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NUTRITION AND HYPERTENSION IN BLACKS AND OTHER MINORITIES

EDITED BY
CYRIL O. ENWONWU

Annual Nutrition Workshop Series
Volume II

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Meharry Medical College

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Nutrition and Hypertension in Blacks and Other Minorities

Editor

Cyril O. Enwonwu, Sc.D, Ph.D., M.D.S.
Director, Center for Nutrition
Professor of Family and Preventive Medicine
Professor of Community Health and Preventive Dentistry
Meharry Medical College
Nashville, Tennessee, USA

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PREFACE

Hypertension is a major risk factor for cardiovascular disease and stroke, which are among the leading causes of premature death in technically developed, affluent countries. The principal demographic features of hypertension (HBP) in the USA are now reasonably well defined. Almost 40 percent of adult blacks in this country suffer from HBP, compared with only 28 percent of the total US adult population. Several studies indicate that nationwide, blacks are 2-5 times at greater risk for HBP than whites matched for age and sex, especially after the second decade of life, and are much more likely than whites to have secondary complications from uncontrolled HBP.

Until relatively recently, the primary approach to the clinical management of HBP has been the use of hypotensive drugs, most of which have undesirable side effects. It is, however, becoming increasingly clear that despite the complexities of the relationship between nutrition and cardiovascular physiology, dietary habits and nutritional factors are intimately involved with the onset and course of HBP. Regrettably, hardly any workshop/conference in recent years focused specifically on the dietary habits of blacks and other minorities, and how these might relate to markedly disproportionate susceptibility of some of these population groups to HBP. Our workshop was intended to fill this disturbing gap.

The workshop was held at the Kresge Learning Resources Center Meharry Medical College on October 26-28, 1989, and was attended by one hundred and thirty eight registered participants, including a few from outside the United States. During the three-day workshop, invited experts deliberated extensively on the physiological regulation of blood pressure, the unique biological characteristics and dietary patterns of blacks and other minorities, prevalence of hypertension in U.S. Blacks and native Americans, roles of specific macro - and micro - nutrients in the genesis of HVP, obesity and HBP, and the childhood antecedents of HBP in adult life.

Financial support for this timely, important workshop was provided by the General Foods Fund, Inc., United States National Institutes of Health, Best Foods, The Phillip Morris Companies and Proctor and Gamble Company. Meharry Medical College is very grateful for the generous support.

Cyril O. Enwonwu

ADDRESS OF WELCOME

David Satcher, M.D., Ph.D.
President, Meharry Medical College

Thank you very much Dr. Johnson, Dr. Enwonwu, and members of the planning committee for this conference. On behalf of the entire Meharry Medical College family, I like to take this opportunity to welcome all the participants to Meharry. If you look at your program, I am allowed almost 30 minutes to give the welcome address. You probably know that it does not take that long to welcome you. I think what I will like to do for a few minutes is to try and place this conference in perspective as it relates to our institution first and also as it relates to what I consider to be a tremendous challenge which we face in this country.

A few weeks ago, the first Monday in October, we celebrated our 113th convocation at Meharry Medical College. So we have been around since 1876. During these years, we have been trying to carry out a special mission; a mission which targets the underserved in this country. We are concerned about access to health care for the underserved in this country whether they be in rural areas or in the inner cities or wherever. We are also concerned about access to health professional careers for blacks and other minorities, and I think the role which this institution has played in carrying out that mission is one that is well known. In 1980, the Robert Wood Johnson Foundation did a report on Meharry in which among other things it pointed out that more than 40 percent of the black physicians and dentists in this country had been educated at Meharry Medical College. I think, perhaps, more surprising, they found that 43 percent of the black faculty members of medical schools in this country at that time were graduates of Meharry. Meharry's mission, I think, is certainly reflected in those data. They also found that three out of every four of Meharry's graduates over the ten years prior to that report had in fact gone to practice in underserved rural and inner-city communities.

That is the mission to which this institution commits itself and The Nutrition Center is a very important part of the mission. In 1982, we embarked upon a program which we call "The Plan for Academic Renewal." It was first and foremost a fundraising campaign. The goal was to raise $33 million, but the targets were to strengthen the faculty in size and depth, upgrade our library, provide scholarships for students, do some much needed renovation, and to develop research centers of excellence. It was a very successful campaign. Financially, we exceeded our goal, but we also were able to develop some very important research centers of excellence, including The Nutrition Center which was funded by the General Foods Fund Inc., early in 1986.

The Nutrition Center has as one of its major goals, assuring that every student at Meharry Medical College, whether that student is in the School of Medicine, the School of Dentistry, the School of Graduate Studies or the School of Allied Health, leaves here with some understanding of basic nutrition and how it impacts upon the health of people and specifically how it influences various

disease processes, including hypertension. We feel that The Nutrition Center has been very successful in influencing the curriculum of this institution. More importantly, General Foods feels that it has been one of the most successful programs that it has funded in terms of impacting upon the curricula of medical schools and in helping professional schools in this country.

So we welcome you here with that perspective. We are really trying to make a contribution to health care where it is most needed, and to better prepare our students to understand the relationship between nutrition and health.

Dr. C. W. Johnson, who is our Vice President for Academic Affairs and Executive Vice President, is in his last year in both positions after spending more than 40 years here at Meharry. In the early 1970s he started a graduate school at Meharry Medical College because he felt the need to really influence more students to go into academic careers. To point out how serious that problem is, today, less than 2 percent of faculty members throughout this country in schools of medicine are black and if you were to remove Meharry Medical College and Howard University from the picture, it would be approximately 1.4 percent.

We started our graduate school in 1972. Since that time, we have graduated between 5 and 10 percent of all blacks receiving doctorate degrees in the biomedical sciences. That is a very serious challenge facing us in this country and we are hoping that continually Meharry Medical College will successfuly impact upon that. Some of our graduate students are here today. The Nutrition Center has already had a major impact on the research programs of this institution.

Last summer we had the first summer of our minority research center of excellence, a program funded by the National Science Foundation. In addition to strengthening research at Meharry, this program allows us to reach out in the community to junior high schools, high schools, colleges and to try to influence young people very early toward careers in biomedical research.

So welcome to Meharry Medical College and we hope that those of you who are here in the audience will gain significantly from this conference and those of you who are guest speakers will feel that you have made an important contribution to a very important mission.

Thank you.

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Vice President for Academic Affairs

First Scientific Session

Chair **Cyril O. Enwonwu, Sc.D., Ph.D., M.D.S.**

OVERVIEW OF HYPERTENSION

Arthur C. Guyton
Department of Physiology and Biophysics
University of Mississippi Medical Center
Jackson, MS

The title of this workshop denotes that it is concerned with nutrition and specifically with hypertension in blacks and other minorities. Though I am certain that there are no conceptual differences between the causes of hypertension in blacks, other minorities, and whites, nevertheless we are all aware of the higher incidence of hypertension among blacks in United States society, and we are also aware of the suspicion that various aspects of nutrition might play a role in this.

For the purposes of today's workshop, we are specifically concerned with the basic causes of hypertension, most importantly the relationship of salt intake to hypertension. Our own research work has addressed this very issue, for we have studied especially the intertwining roles of salt intake and kidney function in the genesis of hypertension. Therefore, I shall limit my remarks to a discussion of these specific issues. I believe that I am safe in saying that a major share, if not most, of this Workshop will be concerned with this aspect of hypertension.

How Does the Kidney Function with the Circulation to Control Blood Volume, Cardiac Output, and Arterial Pressure? Pressure Diuresis and Pressure Natriuresis

Let us begin our discussion by explaining the role of the kidney in controlling blood volume, cardiac output, and arterial pressure. Figure 1 illustrates the relationship of the renal nephron to the circulation. If one will think about this diagram for a moment, one will see that any change in the arterial pressure is reflected by a change in the pressure in the renal glomerulus. Therefore, a rise in systemic arterial pressure will cause immediate greatly increased filtration of fluid through the glomerulus into the renal tubules. As demonstrated in perhaps a thousand different laboratories, this causes very rapid flushing of both water and salt through the renal tubular system and an increase in urinary output (1). This phenomenon is called pressure diuresis for the effect of pressure on water output and pressure natriuresis for the effect of pressure on salt output.

Figure 2 gives the results of an experiment in dogs that illustrate this phenomenon of pressure diuresis-natriuresis as well as the effect of this on the control of cardiac output, urinary output, and arterial pressure (2). In this experiment, the nervous systems of the dogs had been destroyed so that the nervous reflexes would not oppose any changes in circulatory hemodynamics. Then, after an hour long control period, a blood transfusion was given to each of the animals equal in volume to about 40 percent of the animal's original volume. Note in the upper panel an acute increase in cardiac output of about 3-fold, and in the lower panel an acute increase in arterial pressure to about 125 percent above the normal level. Thus, the primary effect of the increased blood volume was, first, increased pumping by the heart to give a greatly elevated cardiac output, and this in turn increased the arterial pressure as well. However, now observe the middle panel showing the effect of the elevated pressure on urinary output. In this case, the rise in arterial

pressure caused a 12-fold increase in urinary output, which was an excellent illustration of the phenomenon of pressure diuresis-natriuresis. Thus, immediately upon elevation of the arterial pressure, the kidneys began to eliminate much of the excess volume. And, note also that excess volume continued to flow into the urine as long as the arterial pressure remained above normal. Therefore, the pressure diuresis-natriuresis mechanism functions as a typical negative feedback control system to eliminate excess volume when the arterial pressure is above normal; then, as the volume is eliminated, the cardiac output, the arterial pressure, and the urinary output all return to normal.

The "Infinite Gain" Feature of the Pressure Diuresis-Natriuresis Mechanism for Control of Arterial Pressure

The immense importance of the pressure diuresis-natriuresis mechanism for control of arterial pressure can be appreciated if one recognizes that the mechanism returns the pressure all the way to normal, not simply part way to normal, after an increase in blood volume. This is illustrated in Figure 2 which shows the arterial pressure returning all the way back to normal, not merely part way back. Thus, it is said that this feedback mechanism for control of arterial pressure has "infinite gain." That is, the mechanism has an infinite capability to correct fully the abnormal pressure, not merely to correct it partially. This principle of infinite gain can be understood much more fully by referring to Figure 3. The curve in this figure is called a renal function curve (3). It illustrates the effect of different levels of arterial pressure on renal output of fluid. Essentially the same curve applies also to sodium output, which increases in almost like manner with increasing pressure. Note specifically that when the arterial pressure falls to about 50 to 60 mmHg, urinary output ceases. At the other extreme, an increase in arterial pressure to double normal (to 200 mmHg) increases the urinary output 7 or 8 - fold.

Now, let us superimpose onto the renal function curve in Figure 3 a line denoting the level of net fluid intake (fluid input minus fluid losses besides through the kidneys). If the fluid intake remains exactly constant, and the renal function curve also remains exactly constant, only one pressure level will give a urinary output of fluid (or salt) exactly equal to the intake. In the figure, this is called the "equilibrium pressure"; in the normal adult human being the equilibrium pressure level averages very near to 100 mmHg.

Obviously, a person cannot live indefinitely with more intake of fluid and salt than output, or otherwise he would become bloated and die of edema. Conversely, one cannot live indefinitely with more output of fluid than intake, or otherwise he would become dehydrated and eventually die of hypotension. Therefore, one sees the extreme importance of the equilibrium pressure level shown in Figure 3. For instance, if the arterial pressure rises to even a few mmHg greater than the 100 mmHg equilibrium pressure, the output will be greater than the intake. As a result, the fluids of the body will begin to decrease, and they will never stop decreasing until the output again equals the intake. This will not occur until the pressure falls back exactly to the 100 mmHg level. Conversely, if the arterial pressure should fall below normal, then fluid intake becomes greater than output. As a result, the blood volume will increase, the cardiac output will increase, and the arterial pressure will increase until the output again equals the intake. Therefore, always the arterial pressure reapproaches the equilibrium pressure level.

The Two Determinants of the Long-Term Arterial Pressure Control

Since the renal function curve and net level of fluid intake are the two factors that determine the equilibrium pressure level in Figure 3, then it is clear that the long-term level of arterial pressure cannot be changed from normal except by one of two means: (a) by changing the level of fluid intake, or (b) by changing the renal function curve (3).

If the renal function curve is shifted to the right in Figure 3, then the equilibrium pressure also will shift to the right--that is, the long-term level to which the arterial pressure will be regulated will be increased. Conversely, if the renal function curve is shifted to the left, the long-term arterial pressure will be regulated to some level below normal.

Now, note in Figure 3 the effect of increasing fluid intake. This will raise the level of the fluid line, and one can see that the regulated level of arterial pressure will be increased. But a decrease in the fluid intake line will decrease the pressure.

Thus, one can state that the two determinants of the long-term level of arterial pressure are:
(1) the level of intake of fluid and electrolytes (mainly salt);
(2) the ability of the kidneys to excrete the fluid and electrolytes at different pressure levels, characterized quantitatively by the renal function curve.

Hypertension Caused by an Abnormal Renal Function Curve or by Increased Fluid and Salt Intake

Figure 4 illustrates 6 representative renal function curves for 6 different functional states of the kidneys.

In addition, two lines are drawn to illustrate two different levels of salt and water intake. The renal function curves in this figure are a type called the "salt-loading renal function curve." Such curves are determined by placing an animal or a human being on a very low salt intake for a few days and measuring the arterial pressure level after equilibrium is established (usually in about three days). Next, the salt intake is elevated to a new level, and again the pressure is measured after equilibrium. Gradually over a period of many days, multiple points are determined along the "salt-loading" renal function curve by progressively increasing the salt intake in stages and recording the relationship between salt intake and the long-term arterial pressure level that it causes. The steep curve to the left in Figure 4 is the normal salt-loading renal function curve. At normal salt intake, the intake line equilibrates with this normal renal function curve at Point A, at an arterial pressure of 100 mmHg. Now note that at the high salt intake level (the upper line), the intake line equilibrates with this same normal renal function curve at a pressure level of 102 mmHg. Therefore, when the two kidneys are absolutely normal, even marked changes in salt intake will cause very little change in arterial pressure. In fact, in one study in human beings in which the salt intake was changed from a low of 10 mEq/day to a high of 1500 mEq/day--a 150-fold change in salt intake--the arterial pressure increased only 17 mmHg (4). And in a study in dogs, an increase in salt intake of approximately 50-fold increased the long-term mean arterial pressure by only 4 mmHg (5).

Yet, if we look at the other renal function curves in Figure 4, we see that some of these equilibrate with the salt intake lines at hypertensive levels (3). Some types of renal disease, such as constriction of the renal arteries (designated in the figure as "Goldblatt") will cause the whole renal function curve to shift rightward to high pressure levels but still with a very steep slope. In this case, the regulated arterial pressure level will be high at both normal and high salt intakes.

On the other hand, other functional states of the kidneys show a sloping renal function curve. For instance, this occurs when excess amounts of angiotensin or aldosterone are circulating in the blood. At low salt intakes, the arterial pressure may be nearly normal, and yet at high salt intakes the arterial pressure can be quite hypertensive. Therefore, one can see why the salt intake will affect blood pressure much more in some people - those who have sloping renal function curves - than in other persons - those who have steep renal function curves.

The Unimportance of Changes in Total Peripheral Resistance in Pressure Control

One of the consequences of the pressure diuresis-natriuresis mechanism for pressure control is that, as long as the renal function curve does not change and the levels of fluid and salt intake do not change, changes in total peripheral resistance will not affect the long-term arterial pressure level. The reason for this is very simple. Any time the pressure rises above normal, the kidneys will eliminate more water and salt than normally. And there will be continual loss of water and salt until the arterial pressure falls to that exact level that will once again balance output of water and salt with intake. If the renal function curve has not changed, this pressure level will be at exactly the normal pressure, as illustrated in Figure 3.

This principle that total peripheral resistance might be unimportant in pressure control seems to be at odds with what we know about hyperten-

sion, for most persons with hypertension, especially those with essential hypertension, have high total peripheral resistance. We will discuss this later, but for the time being let us observe Figure 5. This figure illustrates multiple clinical conditions in which the total peripheral resistance varies from a low of about 50 percent of normal up to more than 160 percent of normal (3). Plotted in this figure are the approximate arterial pressures and cardiac outputs in these conditions at the different total peripheral resistances. Observe that the arterial pressure in each condition is either normal or very near to normal. On the other hand, the cardiac output is almost exactly inversely proportional to the total peripheral resistance. At a total peripheral resistance of 50 percent of normal, the cardiac output is 200 percent of normal. But at the other extreme, at a total peripheral resistance of 160 percent, the cardiac output is almost 40 percent below normal. Thus, primary changes in total peripheral resistance control cardiac output, not arterial pressure.

However, the clinical conditions in Figure 5 have an essential difference from those other clinical conditions that cause hypertension. In all of the conditions in Figure 5, the renal function curves are in the normal pressure range because these conditions do not significantly affect renal function. On the other hand, in all hypertensive patients in which the renal function curve has been measured, it has been found to be abnormal and shifted to a much higher arterial pressure range; thus the kidneys are not functioning normally to eliminate water and salt (6).

Yet, we still need to address the question: Why is the total peripheral resistance increased far above normal in almost all patients with essential hypertension? We shall discuss this in the following section.

The Role of Whole-Body Autoregulation to Increase the Total Peripheral Resistance in Hypertensive States

The principle of whole-body autoregulation means simply that the local tissues in virtually all parts of the body control their own local blood flows despite changes in arterial pressure level. That is, if the arterial pressure is increased, this usually causes only a temporary increase of the local blood flows above the normal range. Over a period of time, minutes in some instances, days or weeks in other instances, each tissue readjusts its own local vascular resistance until the blood flow returns almost completely to the normal level despite continued elevated pressure.

There are multiple feedback mechanisms in the tissues that cause local autoregulation of blood flow. One of these, called the metabolic mechanism, is the following: When the arterial pressure rises and causes too much blood flow through a tissue, this delivers more nutrients to the tissues than are required for normal metabolism, and it also removes more waste products than usually. The presence of excess nutrients in the tissues - especially of oxygen - and diminished quantities of some waste products such as carbon dioxide that normally dilate the blood vessels, all these acting together, cause the peripheral blood vessels to constrict and the flow to return toward the normal rate (7,8). In some highly metabolic tissues this acute response occurs within a few seconds to a few minutes and returns the blood flow near to normal despite continued elevation of the pressure. However, in other tissues, especially those that are not highly metabolic, the acute return of the blood flow is very slow and often very incomplete. However, an additional mechanism for return of the blood flow to normal is not simply vasoconstriction but instead actual structural changes in the vessels occurring over a period of weeks, months, and years to make them permanently smaller in internal diameter. These structural changes are called "long-term autoregulation" in contrast to the acute response which is called "short-term autoregulation." Generally, long-term autoregulation is many times more potent in returning the blood flow back toward the normal level than is short-term autoregulation.

In some tissues, the autoregulation process employs nonmetabolic mechanisms. For instance, in the kidneys, a phenomenon called tubuloglomerular feedback is the most important means by which renal blood flow is autoregulated. In this instance, it is not delivery of too much nutrients to the tissues that causes the autoregulation, but instead flow of too much fluid in the renal tu-

bules. The excess fluid acts on the macula densa at the beginning of the distal tubules, and a vasoconstrictor feedback response from this structure directly to the renal arterioles reduces the renal blood flow when the arterial pressure rises too high and causes too much glomerular filtrate (9). Regardless of the mechanism, virtually every tissue in the body will increase its resistance whenever the arterial pressure rises too high. This causes the total peripheral resistance to increase, because the total peripheral resistance is an algebraic sum of all the local resistances in the body. Consequently, it does not matter what the initial cause of hypertension is, the long-term autoregulation mechanism will generally bring the cardiac output almost all the way back to normal when the arterial pressure is elevated, and, in doing so, it increases the total peripheral resistance as well. Therefore, we can express the relationship between total peripheral resistance and the state of hypertension not that an increase in total peripheral resistance causes hypertension but instead that the development of hypertension causes secondary increase in total peripheral resistance. There is an exception to the rule that the increased total peripheral resistance in hypertension results secondarily from autoregulation. This occurs when some extraneous factor increases the total peripheral resistance and also shifts the renal function curve to a hypertensive level at the same time. For instance, let us assume that some vasoconstrictor effect throughout the body increases all of the peripheral resistances, thus increasing the total peripheral resistance. At the same time, let us assume that the same vasoconstrictor influence constricts the different arterioles of the kidneys, which shifts the renal function curve to a much higher pressure level and causes hypertension. In this instance, the increase in total peripheral resistance tends to reduce blood flow, and this counterbalances the effect of the high arterial pressure to increase blood flow. Therefore, the local flows do not change and are already autoregulated to their normal levels. Thus, one might say that autoregulation does not in this case cause the high total peripheral resistance. Yet, in another sense, one might also say that the autoregulation mechanism still tests the local tissue blood flows and determines that autoregulation is not needed. But, if there is any imbalance between the renal effect to raise the pressure and the peripheral flow, and the peripheral resistance effect to counterbalance an increase in flow, the autoregulation mechanism will still make up the difference.

An Experimental Study Illustrating the Role of Whole Body Autoregulation - Volume-Loading Hypertension

Figure 6 illustrates in summary form many of the principles that we have thus far discussed, including especially the role of whole body autoregulation to increase the total peripheral resistance and also to return the cardiac output almost exactly to normal during the hypertensive state. In the experiments summarized in this figure, about 70 percent of the kidney mass in several groups of dogs had been removed in advance, and the animals had already recovered (10-12). This removal of kidney mass caused the renal function curve to slope markedly toward higher pressure levels as salt intake was increased. At zero day in the experiment, the salt intake was increased to about 5 times normal. Because of the reduced renal mass and the markedly sloping renal function curve, the kidneys began to retain salt and water. Therefore, in rapid succession the extracellular fluid volume, blood volume, and cardiac output all rose to levels far above normal. Along with this, the arterial pressure began to rise as well, but during the first few days the baroreceptor reflex mechanism kept the pressure from rising as rapidly as the cardiac output rose. Indeed as illustrated by the next to bottom panel, the total peripheral resistance actually fell for the first few days until the baroreceptor reflex adapted (that is, lost its effectiveness because of resetting of the baroreceptor stretch receptors). Then, after three or four days, the long-term autoregulation mechanism began constricting the peripheral blood vessels and returned the cardiac output toward normal. This simultaneously increased the total peripheral resistance as well. Thus, over a period of several days to weeks, the cardiac output returned virtually all the way back to normal while the total peripheral resistance increased. Yet, during all this time, the hypertensive level of arterial pressure was maintained.

Thus, this experiment illustrates that the initial cause of volume-loading, salt-loading hypertension is elevated cardiac output, not increased total peripheral resistance. If one will follow through the logic of this experiment, one will also see that the rising blood volume increases the drive by the heart to pump blood. Then, hypertension develops, and blood flow through all the tissues becomes far greater than normal. This increased flow through the tissues then causes a secondary increase in total peripheral resistance and return of the cardiac output back to normal. In other words, the hypertension comes first and then the increased total peripheral resistance, not the other way around. This is an extremely important principle. It is especially important when one considers the role of salt in causing hypertension because so many researchers have been searching in vain for direct effects of salt on the peripheral blood vessels as the cause of salt-loading hypertension.

Role of the Renin-Angiotensin System in Long-Term Control of Arterial Pressure - It Lets Us Eat Small Amounts of Salt or Large Amounts of Salt

Earlier in this paper I pointed out that multiple experiments have shown that both human beings and animals with normal kidneys change the arterial pressures only very, very slightly even with tremendous changes in the level of salt intake. However, this is not true when the renin-angiotensin fails to function. Let us explain.

Figure 7 illustrates three salt-loading renal function curves (3). The centralmost curve was recorded in a group of normal dogs in which the salt level was increased every few days while the relationship between mean arterial pressure and urinary output of sodium was recorded to generate the curve. The other two curves were recorded in dogs after their renin- angiotensin systems had been rendered non-functional. For the left-hand curve, ther renin-angiotensin system was rendered non-functional by giving captopril (SQ-14,225) which eliminated the capability of forming angiotensin II. For the right-hand curve the renin-angiotensin system was rendered non-functional by continuous intravenous infusion of angiotension II. This suppressed the animal's own renin-angiotensin system to a non-functional status but it allowed a high level of angiotensin to persist in the blood during the entire experiment.

Finally, note the numbers in parentheses on the figure. These are calculated levels of angiotensin II at the different stages in generating the three renal function curves.

Now, observe from the two curves with fixed angiotensin levels, either zero angiotensin level after captopril (SQ-14,225) or high angiotensin level during angiotensin infusion, that changing the rate of sodium intake changed the arterial pressure about 40 mmHg. Also, in the presence of high angiotensin, the entire curve was shifted to the right to about 40 mmHg higher pressure levels. This means that with high circulating angiotensin, approximately 40 mmHg additional pressure was required to cause the same amount of salt excretion.

On the other hand, the normal renal function curve (the middle curve) was very steep. Yet, note that at the top of the normal curve, the circulating level of angiotensin was 0, which was the same level of circulating angiotensin for the entire captopril curve. At the bottom of the normal renal function curve, the circulating angiotensin was about 3 times normal, which was near to the level of circulating angiotensin for the "angiotensin" curve. Therefore, in effect, during the low salt state, the normal animals' kidneys were operating on the bottom of the high angiotensin curve. But during the high salt state, the normal animals' kidneys had now shifted to operate on the 0 angiotensin curve.

Thus, thinking through this set of experiments and its implications, one can see that the renin-angiotensin system serves as a negative feedback mechanism to prevent marked changes in arterial pressure despite tremendous changes in salt intake. For instance, in recording the normal curve of Figure 7, there was a change in salt intake of about 50-fold from the bottom of the curve to the top, and yet the arterial pressure changed by only 4 mmHg (5). The other two curves in this figure illustrate that when the renin-angiotensin system was not allowed to function, the same change in salt intake caused about 40 mmHg change in arterial pressure in each instance.

Therefore, what is the value of the renin-

angiotensin system in normal day-to-day arterial pressure control? The answer to this is that many members of the human population live in areas where there is virtually no salt in the diet, such as in some inland areas far from the sea where salt is scarce. Yet, others subsist almost entirely on fish products from the sea and therefore have an exceedingly high salt intake, such as much of the population of some coastal areas of Japan. The salt intake can vary perhaps as much as 100-fold, and yet, in early life the arterial pressures of all these persons are near the same level.

Probable Effect of Chronic High Salt Intake to Shift the Renal Function Curve into the Hypertensive Range

Even though very large increases in salt intake over a period of days, months, or even a few years do not seem to cause a large increase in arterial pressure in human beings, nevertheless, many long-term animal experiments as well as epidemiological studies in human beings demonstrate a definite correlation between salt intake and the eventual level of arterial pressure. Therefore, there is much reason to believe that chronic intake of high levels of salt causes hypertension despite the normal function of the renin-angiotensin system to compensate for high salt intake. At present, very little is known about why this occurs. Yet, on the basis of what we do know, it is likely that it is the result of renal structural changes that permanently shift the salt-loading renal function curve into the hypertensive range. A clarification of this problem is of the highest priority on the agenda for future hypertension research.

Summary

The goal of this paper has been to present those features of hypertension specifically related to the most important nutritional problem in hypertension, the problem of salt intake.

As long as the kidneys and the renin-angiotensin system are entirely normal, salt intake can vary tremendously, perhaps as much as 100-fold, without driving the mean arterial pressure out of the normal operating range. Yet, this is not true when the kidneys are abnormal or when the renin-angiotensin system fails. In either of these cases, the salt-loading renal function curve often slopes to a markedly hypertensive level when the salt intake is increased above normal. Furthermore, there is reason to believe that chronic high salt intake can cause renal structural changes that shift the entire renal function curve permanently into the hypertensive range. Thereafter, the pressure will be hypertensive regardless of low or high salt intake.

An especially interesting finding from studies on salt- and volume-loading hypertension has been that this type of hyper- tension begins with elevated cardiac output. After a few days the cardiac output returns to normal while the total peripheral resistance rises secondarily to a high level. Thus, the hypertension has a secondary effect to cause high total peripheral resistance, not the other way around. The importance of this concept is that we do not need to search for a direct effect of high salt on peripheral vascular resistance to explain salt-loading hypertension.

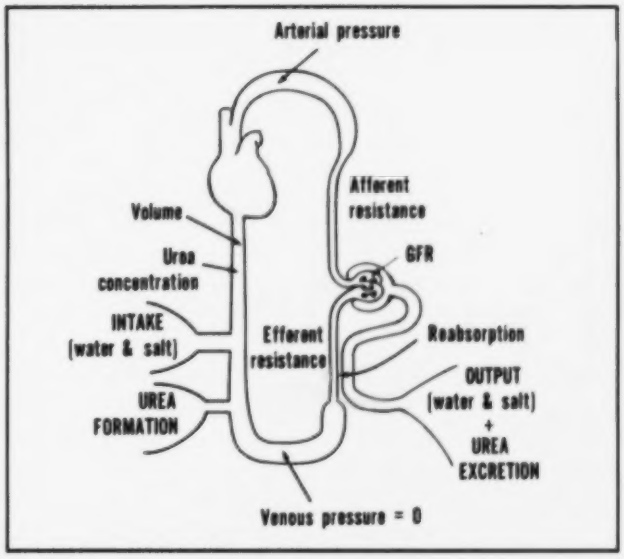

Figure 1. A simple model of the circulatory system along with a renal nephron, illustrating the basic structures for control of arterial pressure diuresis and pressure natriuresis. [Reprinted from Guyton (3)].

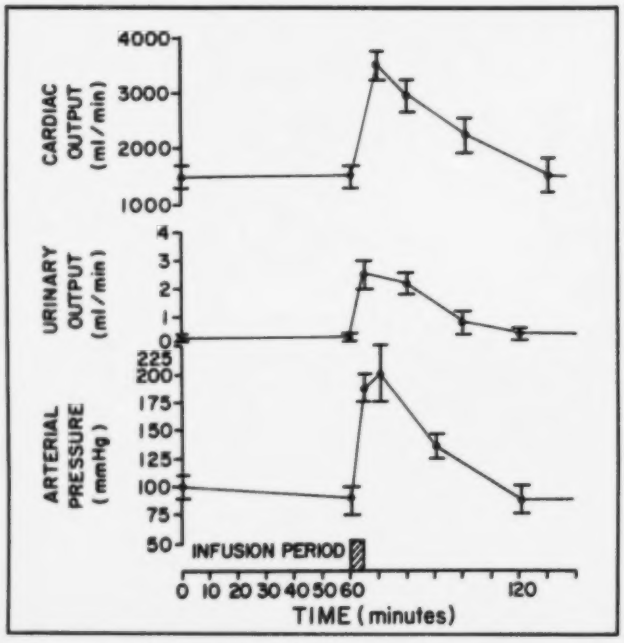

Figure 2. Demonstration of pressure diuresis-natriuresis following transfusion of a large volume of blood into dogs whose nervous systems had been destroyed. The volume of blood transfused was equal to about 40 percent of the animal's own blood volume. [Reprinted from Guyton (3), after Dobbs.]

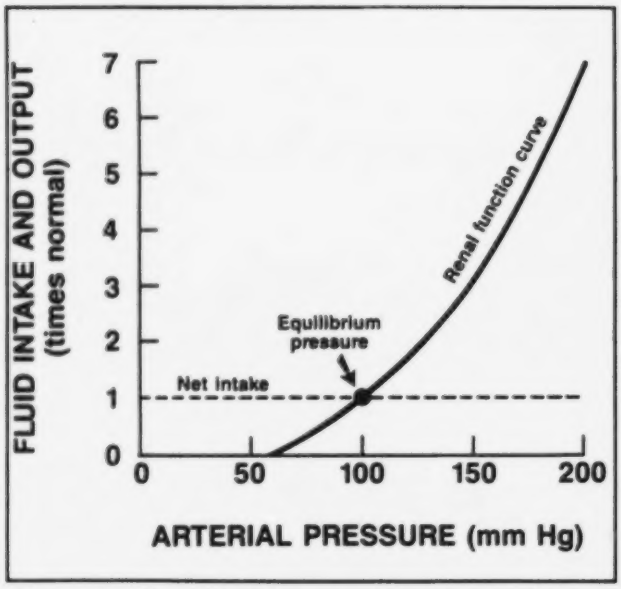

Figure 3. A method for equating the renal function curve with the net fluid intake. The point of intersection, called the "equilibrium pressure," is the pressure level at which long-term arterial pressure is controlled. [Modified from Guyton (3).]

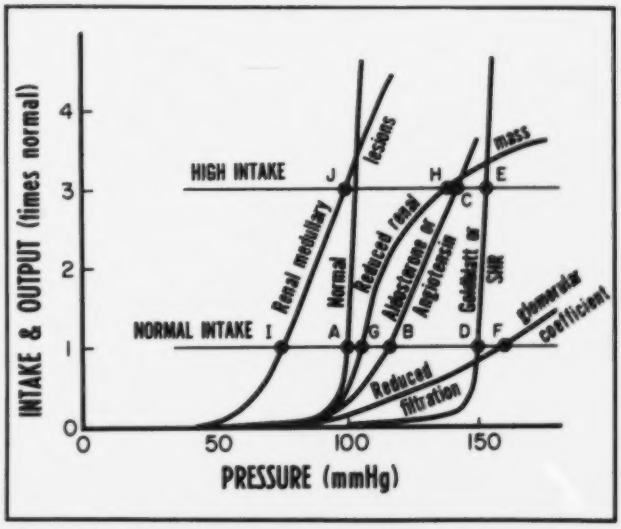

Figure 4. Graphical analysis of long-term arterial pressure regulation for different functional states of the kidneys at normal salt intake and at high salt intake. [Reprinted from Guyton (3).]

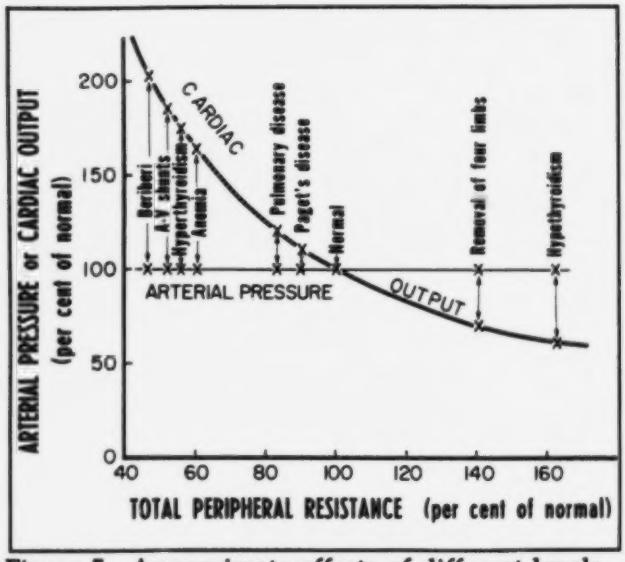

Figure 5. Approximate effects of different levels of total peripheral resistance, as found in different clinical conditions, on arterial pressure and cardiac output. In each of these clinical conditions the renal function curve operates in the normal pressure range. [Reprinted from Guyton

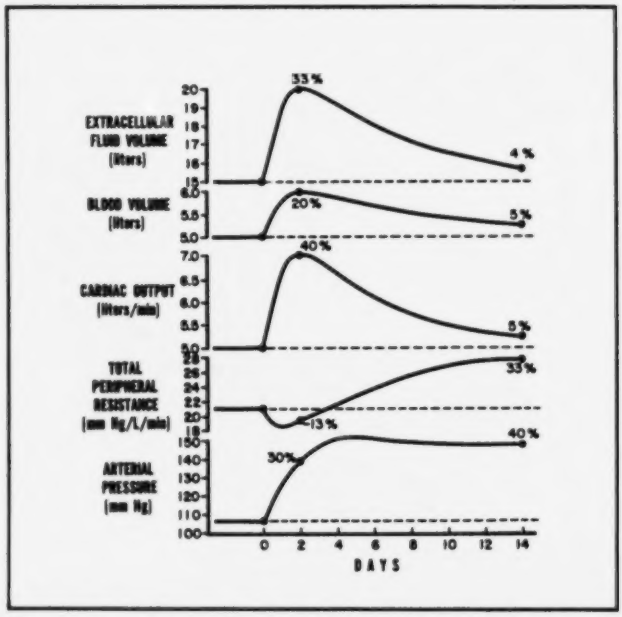

Figure 6. Approximate changes in extracellular fluid volume, blood volume, cardiac output, total peripheral resistance, and arterial pressure during the development of volume- loading hypertension as studied in a series of dog experiments. Several weeks prior to experimentation approximately 70 percent of the kidney mass had been removed. Then, on day 0, the salt intake was increased to about 5 times normal by continuous infusion of isotonic saline. [Modified from Guyton (3).]

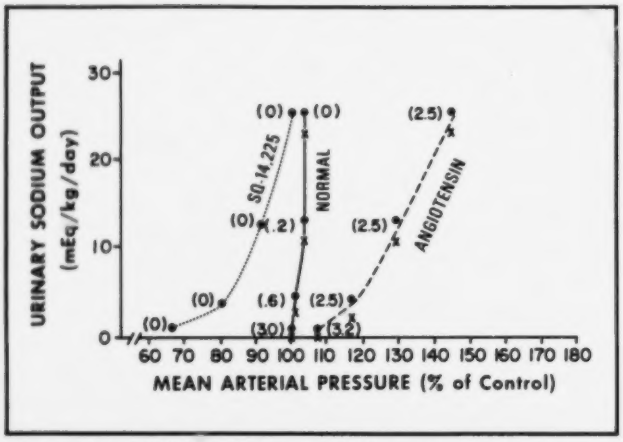

Figure 7. Salt-loading renal function curves recorded in dogs under three different conditions: (a) With 0 circulating angiotensin after giving captopril (labeled SQ-14,225); (b) in normal dogs in which the circulating angiotensin level increased at low salt intakes and decreased at high salt intakes; and (c) in dogs receiving a continuous infusion of angiotensin II to maintain a high level of angiotensin at all times [Reprinted from Guyton (3), after DeClue and Hall.]

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THE UNIQUE BIOLOGICAL CHARACTERISTICS OF BLACKS AND OTHER MINORITIES

Joseph C. Edozien
Department of Nutrition, School of Public Health
The University of North Carolina at Chapel Hill
Chapel Hill, NC

Introduction

The pattern of human chronic diseases has shown remarkable changes during the last five decades. The population in the industrialized countries have rapidly passed through phases of hypertensive disease and diabetes to the current concerns about coronary heart disease and cancer. The affluent in the lesser developed countries are going through the same cycle. That the changes can occur quite rapidly is illustrated by the current epidemic of diabetes among the Pima Indians in Arizona (1).

There are some indications but very little conclusive evidence that this chronic disease cycle is related to changes in food habits and life style. But the nature of the connection is still unclear in spite of much research effort on the subject. A large amount of published data indicates, for example, that obesity is an important risk factor for hypertension, diabetes, and possibly, coronary heart disease. This consistent finding suggests that an understanding of the mechanism for the control of the absorption, storage and mobilization of nutrients may elucidate the pathogenesis of these diseases.

It has also been known for some time that there are differences in blood pressure (2), blood hemoglobin concentration (3), calcium balance (4) and body composition (5) between the black and white races. But considerable doubt still exists about the racial or environmental origins of these differences. The continuing lack of adequate information for a satisfactory resolution of these doubts suggested the inclusion of different ethnic groups in an epidemiologic study to investigate the effects of age, sex, race, diet and environmental factors on body composition and plasma hormone levels. The basic concept for this study is summarized in Figure 1. It suggests that age, sex, genetic factors, race, environmental factors and diet might alter, either directly or through hormones, the activity of rate-limiting enzymes that control the absorption, storage, mobilization, metabolism or excretion of nutrients. Apart from adapting each individual to the availability of nutrients, the altered hormones might have other effects on body composition and body function. Furthermore, it is possible that chronic diseases are caused, at least partially, by hormone imbalances within the regulatory system or by excessive changes in hormone function due to persistent high or low intakes of one or more nutrients.

Unfortunately, studies of diet-hormone interrelationships are difficult to design, execute and interpret because of the large number of interacting variables. On the other hand, it is unrealistic to expect that the system can be fully understood by investigating the factors in isolation. This consideration motivated the undertaking of an epidemiologic study of diet/hormone and hormone-hormone interrelationships in free-living human populations having a sufficiently wide range of nutrient intakes to maximize the differences between groups. The expectation was that analyses

of the data might provide some insight into the integral function of the endocrine system and the limits of dietary tolerance permitted by the system.

This report presents the background, methods and results of this epidemiologic study of diet and hormone profiles in free-living human population groups. It also presents results of the analyses of the data to show how the diet controls endocrine function and how the hormones interact with each other in an orderly and functional sequence. The findings were used to develop working hypotheses which were then tested experimentally in the rat and the guinea pig.

Materials and Methods

Eight human population groups were used for the study. They were selected to include different races and populations with a wide range of nutrient intakes and living at three different altitudes. The first group consisted of 230 adult (i.e., >18 years old) volunteers (94 male, 136 female) and included graduate students, faculty and staff of the School of Public Health, University of North Carolina at Chapel Hill. The volunteers included white (Caucasian), black and Oriental (Chinese) subjects. The second group consisted of 62 parents (17 male, 45 female) and 58 siblings of 20 preschool children registered in a Head Start program in Smithfield, North Carolina, USA. They were mostly black but included a small number of white subjects. The third group consisted of 23 male and 25 female Mexican American and black migrant workers who spent the summer of 1979 at a camp near Smithfield, North Carolina.

The fourth group was made up of low-income adults (29 male, 49 female) and 103 children living in a 5 percent random sample of households in Chapare, Bolivia. They lived at an altitude of 100-250 m above sea level, i.e., at about the same altitude as subjects in groups 1, 2 and 3. Five hundred and thirty-one low-income adults (236 male, 295 female) and 745 children living in households participating in a nutrition project in Bolivia made up the fifth group. They constituted a 5 percent random sample of rural families living in three provinces in the State of Cochabamba, Bolivia at an altitude of 2557 m above sea level.

The sixth group consisted of the families of Bolivian professionals (doctors, engineers, lawyers, businessmen). It included 37 adult males, 87 adult females and 118 children living in Cochabamba, Bolivia which has an altitude of about 2557 m above sea level. The seventh group was made up of low-income adults (44 male, 51 female) and 99 children living in a 5 percent random sample of households in two census districts in Oruro, Bolivia (altitude 3706 m). The eighth group consisted of 19 men and 32 women and their children who resided in 40 volunteer households in Colomi, Bolivia, altitude 3200 m above sea level.

All the data and blood for the hormone study were collected in the morning between 0800 and 1000 hours. The subjects were requested to fast overnight. No clinical examinations were carried out but data were obtained only from those who said they were in good health.

The field, clinical and laboratory procedures have been described in full elsewhere (6). Data reduction was by multiple regression analysis (7) or by the T-test as appropriate. When the multiple regression technique was used, the statistical significance of differences between groups was indicated by a P value which is the probability associated with the F-statistic for testing the differences after adjusting for all other independent variables in the regression. The magnitude of the differences between groups was shown either by calculating the mean value for each group after adjustments for all other factors (least square means; LSM; adjusted means) or by the B value associated with each group relative to a selected comparison group. In each case, the differences between groups were considered to be statistically significant for $p<0.05$.

Results

It became evident early in the process of data analysis that race profoundly affected plasma hormone levels. Therefore, in reporting the results, the first, second, and third groups were combined and then subdivided along racial lines into white, black and Oriental races and the Mexican Americans. The Mexican Americans were usually left out in analyses involving race because of the small size of this group. The Bolivians included Indians as well as people of mixed Indian and Eu-

ropean descent but they were grouped together as one race because of the difficulty of making accurate racial identification. Unless otherwise stated only data for adults i.e., >18 years will be reported. The results also showed that the carbohydrate/fat ratio of the diet had a profound effect on body composition and on the plasma levels of several biochemical constituents. Therefore, the data has been presented in descending order of dietary fat level.

The black and white subjects were approximately the same height (Tables 1 and 2). They were taller than the Orientals who were approximately the same height as the high-income Bolivians; the latter group, in turn, were taller than the rural, low-income Bolivians.

The rural low-income Bolivians had smaller triceps and biceps skinfolds than the other groups in spite of having the same body mass index and the same arm muscle area as the high income Bolivians. The triceps skinfolds of the Bolivian professionals were comparable to those of the Americans. The results also indicated that there were significant differences between groups in the TSF/BSF ratio. The Mexican Americans differed from the others in that their mean biceps skinfold was larger than their mean triceps skinfold. The black subjects also tended to have a lower TSF/BSF ratio than the white subjects while all the Bolivian groups had relatively low BSF values i.e., high TSF/BSF ratios.

There were also significant differences between groups in arm muscle area. The Mexican Americans had the largest values followed by the black participants. Men had higher values than women.

The dietary data are presented in Table 3 and 4. The average energy intake of most groups was about 29.0-31.0 kcals/kg/day. However, the Cochabamba group had a much higher energy intake (41.1 kcals/kg/day) whereas the Chapare and Colomi subjects had reduced energy intakes of about 27.5 kcals/kg/day and 24.3 kcals/kg/day respectively.

The high-income Bolivians ate a mixed diet which was similar to that of the Americans except that fat provided about 23 percent of energy compared to 30-40 percent for the Americans. The diet of the rural Bolivians contained still less fat: on the average, fat provided 8-17 percent of the total energy intake, depending on the group.

The lowland peasants obtained their protein mostly from plantains, bananas, cassava and fish. The other peasants ate staple diets consisting of potatoes, wheat, corn, legumes and a small amount of rice except that the peasants in Oruro ate very little corn which they replaced with wheat and quinoa (chenopodium quinoa).

The diet of most groups contained 33-50 g protein per 1000 kcals. The diet of the Oruro and Cochabamba groups contained only about 30 g protein/1000 kcals. Except for the black Americans, who consumed about 0.95 g protein/kg/day, the protein intake of the Americans and the upper income Bolivians was about 1.10 g/kg/day. The Cochabamba peasants who had the high average energy intake of about 41 kcals/kg/day, also ate about 1.19 g protein/kg/day but the mean protein intake of the other peasants was less than 1.00 g/kg/day.

The daily protein intake of all groups appeared to be adequate when assessed by the U.S. recommended allowances (10) or the WHO safe protein allowances (11). Calculation of amino acid intakes from the food consumption of each individual and the amino acid content of foods (12,13) also showed that the amino acid intakes of all groups were adequate by current standards. For example, the lowest average daily intake of tryptophan by any group was 491 mg i.e., about twice the current estimate of 250 mg/day for tryptophan requirement (11). Similarly, the lowest average lysine intake of 2603 mg/day was more than thrice the estimated average requirement of 800 mg/day.

The iron intake of all the Bolivians was high (>20 mg/day) while the diet of the Americans had a low iron content (9-12 mg/day). Most of the iron consumed by the rural Bolivians was derived from potatoes and wheat which were eaten in very large amounts. As a result, only about 13 percent or less of the dietary iron of the rural Bolivians was derived from animal sources compared to 40 percent for the Americans and Bolivian professionals. The plasma iron level of all groups was well maintained except for the participants from Chapare who had low values in spite of their apparently adequate total iron intake.

The diet of the black Americans and all the Bolivian groups had a low calcium density. But, in

spite of the low calcium intakes of these two groups, the plasma calcium concentration of the black Americans was comparable to that of the white Americans and higher than that of the Mexican Americans while the Bolivians had higher average plasma calcium levels than the Mexican, black and white Americans. Among the Americans, the Oriental group had the highest mean plasma calcium level of 10.5 mg/dl.

Compared to the Americans, the diets of the Bolivian groups contained less sodium and more potassium. Salt added to food at the table was not included in the estimates of sodium intake. In general, plasma sodium concentration reflected dietary sodium intake whereas plasma potassium was less influenced by dietary potassium consumption.

Except for the Oruro group, the Bolivians consumed less vitamin A than the Americans; the diet of the Chapare group had a particularly low vitamin A content. Apart from the Orientals, all other groups had relatively low intakes of thiamin. The black and Oriental participants and the rural Bolivians had relatively low intakes of riboflavin while the diet of the Mexican Americans had a very low content of vitamin C.

The hormone data are presented in Table 5 while the plasma concentrations of other biochemical constituents are reported in Table 6. There were substantial differences between groups in plasma hormone levels and other blood and plasma values but within each group, the results were consistent for men, women and children. These differences in the hormone profiles of the population groups are based on age, sex, body weight, race, diet and altitude. A systematic study of the results by visual inspection, simple correlations, one-way analyses of variance and multiple regression analyses was used to determine the relationship of each hormone to anthropometric characteristics, race, altitude, diet and blood measurements.

A few examples will illustrate how testable hypotheses were developed in regard to the complex interrelationships between race, altitude, diet, hormones and other parameters. The plasma concentration of serotonin was positively related to the intake of vitamin C and to the plasma concentration of growth hormone but inversely associated with altitude, the triceps skinfold and the plasma concentration of calcium. Thus the Chapare peasants living at the same altitude as the Americans had a significantly higher plasma serotonin than the Americans (Table 6). This elevated plasma serotonin of the people of Chapare was associated with their low body fat (Tables 1 and 2). The Bolivian peasants living at higher altitudes had similar triceps skinfolds but lower plasma serotonin than the inhabitants of Chapare (Table 1,2 and 6). The Oriental Americans and the peoples of Cochabamba and Colomi illustrate the negative impact of plasma calcium (Table 6) while the Mexican Americans demonstrate the positive effect of vitamin C (Tables 3, 4 and 6).

The high plasma glucagon of the populations of Chapare and Colomi (Table 5) was associated with their low intakes of tryptophan, lysine and niacin (Tables 3 and 4). Compared to the white and Oriental Americans, the black group had low plasma levels of glucagon (Table 5) and tryptophan (Table 6) which could not be explained by dietary factors. These low values were associated with their high plasma concentration of IgG (Table 6) which, in turn, was associated with their high plasma NE level (Table 5).

The findings relating to serotonin and glucagon were used to develop a metabolic map (Figure 2) to explain how race, environmental factors and diet might regulate the metabolism of tryptophan to serotonin and that of tryptophan to niacin. They suggest that growth hormone and vitamin C might enhance the synthesis of serotonin by stimulating tryptophan hydroxylase while calcium and erythropoietin might inhibit the enzyme. Serotonin then feeds back to the enzyme by increasing the synthesis of erythropoietin. They also suggest that NE and glucagon might activate tryptophan oxygenase to enhance the production of niacin which then inhibits the secretion of glucagon. The results for the Oriental Americans indicated that plasma calcium (Table 6) rose significantly when dietary carbohydrates rose above about 50 percent of total energy (Tables 3 and 4). This rise in plasma calcium was associated with an increase in the plasma levels of corticosterone and estrone (Table 5), an increase in plasma Na+ (Table 6), a fall in the plasma concentrations of TSH, T4 and growth hormone (Table 5) and a de-

crease in the plasma levels of serotonin, C3, C4 and IgM (Table 6). Apart from the differences in plasma calcium and the associated variables, the values for the white and Oriental Americans were very similar.

The very low fat intake of the Cochabamba and Colomi groups provided an insight into the role of the adrenocortical system. When the average dietary fat level fell below about 10 percent of total energy intake the plasma concentration of ACTH rose sharply (Table 5). A comparison of the data for these two groups with those of the other two Bolivian peasant groups showed that this increase in plasma ACTH was associated with an increase in the plasma concentration of cortisol (Table 5), a rise in the plasma levels of retinol binding protein, calcium and Na+ (Table 6), a fall in the plasma levels of K+, histidine and serotonin (Table 6) and an increase in diastolic blood pressure (Tables 1 and 2).

The Bolivian data indicated that, through ACTH, dietary fat might reduce the absorption of calcium and/or depress the retention of the mineral. The American results showed that dietary carbohydrates might improve the absorption and/or the retention of the element. Subsequent experimental studies in the rat suggest that carbohydrates might enhance the absorption and/or retention of calcium by stimulating the secretion of parathyroid hormone (PTH). These impacts of dietary fats and carbohydrates on the plasma levels of ACTH, PTH and calcium and the associated metabolic effects are summarized in Figure 3.

The black Americans differed significantly from the white and Oriental Americans. Compared to the Caucasians, the black subjects had elevated plasma concentrations of insulin, norepinephrine (NE) deoxyphenylaline (DOPA), ACTH, cortisol and corticosterone and depressed plasma levels of thyroid stimulating hormone (TSH), parathyroid hormone (PTH) and glucagon (Table 5). They also had elevated plasma IgG, IgA, C3 and C4 and depressed plasma levels of zinc, tryptophan, folacin, cholesterol and potassium. Table 5 shows that, in comparison to the white group, black women had low plasma concentrations of growth hormone, progesterone, estradiol (E2) and estrone (E1) and elevated plasma follicle stimulating hormone (FSH). Black men and women had a large arm muscle area (Tables 1 and 2) but only the women had relatively large triceps and biceps skinfolds (Table 2). The results reported in Tables 1 and 2 also show that the black group had elevated systolic and diastolic blood pressures but depressed blood hemoglobin concentration, hematocrit, mean corpuscular hemoglobin concentration (MCHC) and white cell count (WBC). Unlike the differences between the American and the Bolivians as well as those between the Oriental and white Americans, those between the black and white groups could not be explained by diet. Multiple regression analyses of the data showed that most of the differences were associated with the difference in plasma IgG. Analyses of the data for the black and white subjects who had catecholamine data established that there was a strong positive correlation (r=+0.55) between the plasma levels of IgG and NE. Furthermore, these two parameters and Race 2 (i.e., black race vs all other races together) could be used interchangeably, with the same results, in all regression analyses in which NE was a statistically significant variable. These findings suggest that NE might either modulate the synthesis of IgG or stimulate the differentiation of the cells which produce the immunoglobin. They also indicate that the unique biological characteristics of black people might be due to high plasma concentrations of the catecholamines. The high plasma levels of DOPA, NE and IgG among blacks suggest that they might have inherited a high activity level of tyrosine hydroxylase. The biochemical processes by which NE and/or epinephrine (E) might raise plasma ACTH, retain calcium and Na+, excrete K+, lower plasma tryptophan, suppress glucagon release, impair glucose tolerance, enhance insulin release, depress plasma TSH, expand plasma volume, lower blood hemoglobin concentration, raise blood pressure and suppress ovarian estrogen synthesis are summarized in Figure 4. The high plasma IgG of the Bolivians (Table 6) indicated that they, like blacks, also had high plasma NE. But, unlike the black group, the Bolivians had low diastolic blood pressure. The explanation for this apparent contradiction is that the factors which raise the diastolic blood pressure have strong negative feedbacks to the synthesis and/or metabolism of the catecholamines. Whereas the primary change

in blacks is an increase in plasma catecholamines, the initial impact of dietary factors and low body fat among the Bolivians, especially the peasants, is a fall in diastolic blood pressure. The findings of the epidemiologic study were tested experimentally in the rat and guinea pig (8,9). For example, the hormonal effects of specific amino acids were confirmed by deleting single essential amino acids from the diet of rats for 14 days. The results reported in Table 7 show that loss of body weight caused by deleting any essential amino acid was associated with a fall in plasma insulin. The fall in blood hemoglobin concentration and increase in plasma serotonin associated with the deletion of histidine are consistent with the hypothesis that histidine increased the production of erythropoietin which, in turn, inhibited the synthesis of serotonin. The deletion of leucine produced a fall in the plasma concentrations of ACTH and corticosterone. The fall in plasma corticosterone was associated with low plasma vitamin A, an increase in liver ATPase and a rise in erythrocyte K+.

When tryptophan was excluded, plasma glucagon rose but was returned to normal level by the addition of niacin to the tryptophan-deficient diet. The hormonal changes due to deletion of lysine from the diet can be explained by a primary increase in plasma glucagon. These results are consistent with the conclusion that niacin and lysine are the dietary factors which modulate the secretion of glucagon.

Discussion

The results of this epidemiologic study present clear evidence that there are considerable differences in the hormone profiles of human population groups based on age, sex, body weight, race, diet and environmental factors. They also show that, in addition to being related to nutrient intakes, the hormones interacted with each other in an orderly, functional sequence which might provide a basis for the dietary control of all metabolic processes by controlling the secretion of a few key hormones.

The findings were used to generate alternative models to explain the differences in plasma hormone levels. Rat and guinea pig experiments were then designed and executed to test the hypotheses. The results of these experimental studies were used to select between alternative explanations for the results of the human study. The interpretations reported in Figures 2-4 have taken cognizance of these animal investigations.

The results of this research indicated that the unique biological characteristics of black people might be due to high plasma concentrations of the catecholamines. Their high plasma levels of DOPA, NE and IgG suggest that they may have inherited a high activity level of tyrosine hydroxylase. Other racial differences in plasma hormone levels and in body composition, hematological values and blood pressure can be explained by the difference in plasma catecholamines.The black race might have inherited the high plasma concentrations of the catecholamines partly to increase their production of DOPA for melanin synthesis. They might also have evolved this racial trait to compensate for depressed calcium absorption due to a reduced rate of vitamin D synthesis caused by the reduced absorption of ultraviolet radiation by the black skin pigment. It is also possible that, through a process of natural selection, the black race might have inherited a high plasma level of NE to enhance antibody production against many infective agents in the humid tropics that respond more to humoral immunity than to cellular mechanisms. Since an inverse relationship appears to exist between cellular immunity and the ability to produce antibodies, black people may be more susceptible to infections, such as measles, in which cellular processes have the major role. There has been much discussion regarding the possibility that stress is responsible for the elevated blood pressure in blacks. Although the author does not believe that the elevated plasma catecholamines in black people is caused by stress, it is likely that blacks, because of their increased ability to produce catecholamines, may react to stress in an exaggerated or different manner from other races. Hence, both high blood pressure and altered stress response in blacks may be caused by the same factor i.e., increased ability to produce catecholamines.

To summarize, the results of this study confirm that a number of key nutrients adapted the endocrine system to the diet and the availability of nu-

trients. Environmental and genetic factors e.g., altitude and race also affect plasma hormone levels. The hormones utilization of the nutrients. Each hormone performs only a small number of tasks but produces maximum impact by intervening at a critical metabolic step. Through the effects of nutrients on the endocrine system, diet affects all body functions including the blood pressure and the central nervous system. Therefore, the endocrine system provides the mechanism through which genetic, dietary and environmental factors interact with each other and through which the body becomes adapted to the diet and the environment.

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Table 1
Demographic, Hematological, blood pressure and anthropometric intake data for adult males[1]

TABLE 1

Demographic, hematological, blood pressure and anthropometric data for adult males[1]

Variable	Mexican American	White	Black	Oriental	Bolivian Professionals	Chapare	Oruro	Cochabamba	Colomi
A. Demographic Data									
Country	USA (migrants)	USA	USA	USA	Bolivia	Bolivia	Bolivia	Bolivia	Bolivia
Social class[2]	High	High	High	High	High	Low	Low	Low	Low
Altitude: m	<250	<250	<250	<250	2557	<250	3706	2557	3200
N	15	57	47	15	37	29	44	178	18
Age: yrs	25.4 ± 2.0	30.3 ± 1.0	33.1 ± 1.6	35.7 ± 2.5	37.0 ± 1.8	37.1 ± 2.4	35.6 ± 2.4	40.9 ± 0.8	32.5 ± 2.9
B. Hematological Data									
Hemoglobin: g/dl	17.3 ± 0.2	16.1 ± 0.2	15.4 ± 0.1	16.8 ± 0.3	18.1 ± 0.2	15.3 ± 0.2	18.4 ± 0.3	17.1 ± 0.1	18.4 ± 0.4
Hematocrit: %	49.0 ± 0.6	45.9 ± 0.4	45.6 ± 0.4	47.1 ± 0.5	50.1 ± 0.5	42.5 ± 0.6	51.4 ± 0.7	48.3 ± 0.2	49.1 ± 0.6
MCHC: g/dl	35.3 ± 0.3	35.1 ± 0.2	33.9 ± 0.2	34.9 ± 0.2	36.2 ± 0.2	36.0 ± 0.3	35.9 ± 0.2	35.3 ± 0.1	35.9 ± 0.3
RBC: millions	---	5.05 ± 0.11	5.18 ± 0.15	---	---	---	---	---	---
WBC: thousands	---	6.28 ± 0.15	5.37 ± 0.15	---	---	---	---	---	---
MCV: μm^3	---	94.0 ± 0.3	86.0 ± 1.3	---	---	---	---	---	---
Platelets	---	214 ± 8	229 ± 20	---	---	---	---	---	---
Erythrocyte Na: g	---	6.8 ± 0.2	7.8 ± 0.3	---	---	---	---	---	---
Erythrocyte K: g	---	79.2 ± 2.9	63.0 ± 0.9	---	---	---	---	---	---
C. Blood Pressure Data									
Systolic: mmHg	117 ± 3	115 ± 1	124 ± 3	116 ± 2	112 ± 2	107 ± 9	114 ± 3	117 ± 2	114 ± 5
Diastolic: mmHg	65 ± 3	75 ± 2	86 ± 3	78 ± 2	74 ± 2	57 ± 6	68 ± 4	76 ± 1	76 ± 3.6

Variable	Mexican American	White	Black	Oriental	Bolivian Professionals	Chapare	Oruro	Cochabamba	Colomi
D. Anthropometric Data									
Height: cm	169.9 ± 2.0	176.9 ± 0.9	176.2 ± 1.0	170.4 ± 2.0	168.1 ± 1.6	160.7 ± 1.2	160.5 ± 0.8	161.2 ± 0.4	160.0 ± 0.8
Weight: kg	65.9 ± 2.3	74.0 ± 1.4	74.2 ± 1.9	66.1 ± 2.3	71.3 ± 1.5	58.8 ± 1.2	59.7 ± 1.1	61.3 ± 0.6	64.1 ± 1.6
Body Mass Index	22.8 ± 0.7	23.6 ± 0.4	23.9 ± 0.6	22.7 ± 2.4	25.2 ± 0.5	22.7 ± 0.3	23.1 ± 0.3	23.6 ± 0.2	25.0 ± 0.6
Triceps skinfold (TSF):mm	9.0 ± 1.1	14.7 ± 1.0	12.5 ± 1.3	13.4 ± 1.1	14.8 ± 0.7	7.9 ± 0.5	9.3 ± 0.6	10.0 ± 0.2	10.3 ± 1.2
Biceps skinfold (BSF):mm	10.2 ± 0.8	8.5 ± 0.8	7.0 ± 0.6	6.8 ± 0.8	6.7 ± 0.4	3.7 ± 0.2	3.7 ± 0.2	4.9 ± 0.2	4.8 ± 0.8
TSF + BSF: mm	19.2 ± 1.7	23.2 ± 1.6	19.5 ± 1.4	20.2 ± 1.7	19.6 ± 0.9	11.6 ± 0.6	13.0 ± 0.7	14.9 ± 0.3	15.1 ± 1.1
TSF/BSF: Ratio	0.9 ± 0.1	2.0 ± 0.1	1.8 ± 0.1	2.2 ± 0.2	2.4 ± 0.1	2.2 ± 0.1	2.6 ± 0.1	2.4 ± 0.1	2.2 ± 0.1
Arm circumference: mm	28.9 ± 0.5	29.4 ± 0.3	30.5 ± 0.5	28.9 ± 0.7	29.1 ± 0.4	26.2 ± 0.5	25.4 ± 0.4	26.7 ± 0.2	25.6 ± 1.2
Arm muscle area: sq mm	5459 ± 231	4917 ± 126	5772 ± 219	4887 ± 228	4809 ± 161	4536 ± 169	4069 ± 103	4453 ± 55	4221 ± 258

[1]Results are means ± SE. The results have been arranged in descending order of dietary fat intake (expressed as a percentage of energy intake).

[2]All the Americans and the Bolivian professionals were classified as the high social class groups in analyses involving social class.

Table 2
Demographic, Hematological, blood pressure and anthropometric intake data for adult females[1]

TABLE 2

Demographic, hematological, blood pressure and anthropometric intake data for adult females[1]

Variable	Mexican American	White	Black	Oriental	Bolivian Professionals	Chapare	Oruro	Cochabamba	Colcai
A. Demographic Data									
Country	USA (migrants)	USA	USA	USA	Bolivia	Bolivia	Bolivia	Bolivia	Bolivia
Social class[2]	High	High	High	High	High	Low	Low	Low	Low
Altitude: m	<250	<250	<250	2557	2557	<250	3706	2557	3200
N	15	106	62	14	88	49	51	213	30
Age: yrs	39.2 ± 3.9	28.8 ± 0.7	29.3 ± 1.2	33.1 ± 1.8	35.8 ± 1.5	30.1 ± 1.4	37.9 ± 2.1	40.7 ± 0.8	32.6 ± 2.8
B. Hematological Data									
Hemoglobin: g/dl	14.7 ± 0.3	13.9 ± 0.1	13.1 ± 0.2	13.7 ± 0.2	16.0 ± 0.1	12.7 ± 0.3	16.8 ± 0.2	15.5 ± 0.1	15.7 ± 0.3
Hematocrit: %	42.2 ± 0.8	41.1 ± 0.3	38.6 ± 0.5	40.2 ± 0.8	44.8 ± 0.3	36.4 ± 0.6	47.6 ± 0.5	43.8 ± 0.2	43.7 ± 0.5
MCHC: g/dl	34.7 ± 0.3	33.9 ± 0.2	33.9 ± 0.5	34.6 ± 0.2	35.7 ± 0.1	35.1 ± 0.3	35.2 ± 0.2	35.4 ± 0.1	36.0 ± 0.3
RBC: millions	---	4.44 ± 0.08	4.39 ± 0.07	---	---	---	---	---	---
WBC: thousands	---	5.84 ± 0.15	5.00 ± 0.06	---	---	---	---	---	---
MCV: um^3	---	91.8 ± 0.3	88.0 ± 0.7	---	---	---	---	---	---
Platelets	---	254 ± 14	239 ± 15	---	---	---	---	---	---
Erythrocyte Mas: g	---	5.8 ± 0.2	6.5 ± 0.2	---	---	---	---	---	---
Erythrocyte Ks: g	---	82.1 ± 1.6	76.6 ± 1.3	---	---	---	---	---	---
C. Blood Pressure Data									
Systolic: mmHg	116 ± 3	108 ± 1	119 ± 2	109 ± 3	105 ± 2	102 ± 2	102 ± 2	110 ± 1	98 ± 3
Diastolic: mmHg	65 ± 2	73 ± 1	78 ± 2	73 ± 2	70 ± 1	40 ± 3	46 ± 4	72 ± 1	63 ± 3

Variable	Mexican American	White	Black	Oriental	Bolivian Professionals	Chapare	Oruro	Cochabamba	Colcai
D. Anthropometric Data									
Height: cm	154.8 ± 2.3	165.5 ± 0.7	162.3 ± 1.2	157.4 ± 1.1	153.7 ± 0.7	150.8 ± 0.7	148.6 ± 0.8	150.9 ± 0.3	147.4 ± 0.9
Weight: kg	67.8 ± 4.5	61.7 ± 1.0	67.8 ± 2.1	51.0 ± 1.8	58.3 ± 1.1	58.4 ± 1.3	53.7 ± 1.1	58.0 ± 0.6	57.6 ± 1.4
Body Mass Index	36.8 ± 2.4	22.7 ± 0.5	25.7 ± 0.8	20.6 ± 0.7	24.7 ± 0.5	25.6 ± 0.5	24.4 ± 0.6	25.4 ± 0.3	26.5 ± 0.6
Triceps skinfold (TSF):mm	23.2 ± 3.8	21.1 ± 0.7	24.7 ± 1.5	19.3 ± 1.3	22.0 ± 0.6	16.3 ± 0.7	14.6 ± 0.8	18.4 ± 0.3	16.1 ± 0.9
Biceps skinfold (BSF):mm	26.8 ± 2.0	12.8 ± 0.7	14.4 ± 1.4	11.4 ± 1.2	10.0 ± 0.5	6.9 ± 0.5	5.9 ± 0.4	8.2 ± 0.2	6.2 ± 0.6
TSF + BSF: mm	50.0 ± 5.6	33.9 ± 1.3	39.1 ± 2.3	30.9 ± 2.3	32.0 ± 0.9	22.9 ± 1.0	20.5 ± 1.1	26.6 ± 0.5	22.3 ± 1.3
TSF/BSF: Ratio	0.8 ± 0.1	2.0 ± 0.1	1.7 ± 0.1	1.9 ± 0.2	2.5 ± 0.1	2.6 ± 0.1	2.9 ± 0.1	2.6 ± 0.1	3.0 ± 0.2
Arm circumference: cm	37.3 ± 1.2	27.2 ± 0.3	29.4 ± 0.7	24.9 ± 0.7	27.3 ± 0.4	27.1 ± 0.5	25.4 ± 0.4	27.1 ± 0.2	25.9 ± 0.5
Arm muscle area: sq cm	7175 ± 385	3411 ± 94	3862 ± 113	2834 ± 114	3378 ± 87	3384 ± 116	3488 ± 82	3726 ± 46	3481 ± 108

[1]Results are means ± SE. The results have been arranged in descending order of dietary fat intake (expressed as a percentage of energy intake).

[2]All the Americans and the Bolivian professionals were classified as the high social class groups in analyses involving social class.

Table 3

Daily Nutrient Intake of Adult Males[1]

Variable	Mexican American	White	Black	Oriental	Bolivian (H) Professionals	Chapare (L)	Oruro (L)	Cochabamba (L)	Colomi (L)
N	15	57	47	15	37	28	44	178	19
Energy: kcal	2343 ± 515	2595 ± 119	2024 ± 158	1998 ± 212	2050 ± 105	1381 ± 125	1833 ± 252	2553 ± 108	1380 ± 154
Energy: kcal/kg	35.4 ± 6.5	33.8 ± 1.8	27.9 ± 3.0	29.7 ± 2.7	29.1 ± 1.6	28.7 ± 3.1	33.9 ± 4.6	44.0 ± 1.8	23.4 ± 6.2
Protein: g	82 ± 16	97 ± 5	71 ± 7	81 ± 11	76 ± 4	45 ± 5	59 ± 8	75 ± 3	50 ± 8
Protein: g/kg	1.2 ± 0.20	1.3 ± 0.08	0.9 ± 0.1	1.2 ± 0.1	1.1 ± 0.01	0.9 ± 0.1	1.0 ± 0.1	1.3 ± 0.1	0.8 ± 0.1
Protein: % energy	14.6 ± 1.8	15.2 ± 0.7	14.1 ± 1.1	15.7 ± 1.1	15.1 ± 0.5	12.4 ± 0.8	12.9 ± 0.7	12.2 ± 0.3	14.4 ± 1.4
Tryptophan: mg	1126 ± 233	1143 ± 62	815 ± 78	843 ± 118	1002 ± 59	556 ± 73	640 ± 74	879 ± 33	614 ± 92
Lysine: mg	5655 ± 988	5827 ± 377	4688 ± 535	4350 ± 775	5677 ± 382	2524 ± 351	3204 ± 413	4030 ± 182	2797 ± 638
Histidine: mg	2583 ± 413	2458 ± 144	1892 ± 195	1838 ± 304	2351 ± 153	1197 ± 53	1530 ± 188	1931 ± 80	1315 ± 244
Fat: g	116 ± 30	110 ± 7	74 ± 8	65 ± 9	51 ± 4	20 ± 3	30 ± 7	28 ± 2	15 ± 2
Fat: % energy	42.3 ± 2.0	37.3 ± 1.5	32.2 ± 3.0	28.5 ± 2.5	22.7 ± 1.3	12.9 ± 1.7	13.2 ± 1.7	10.0 ± 0.6	10.3 ± 1.3
Carbohydrates: g	208 ± 47	293 ± 20	230 ± 23	246 ± 24	319 ± 20	252 ± 21	330 ± 40	462 ± 20	260 ± 33
Carbohydrates: % energy	35.6 ± 2.3	44.7 ± 1.9	45.2 ± 2.8	50.4 ± 2.2	61.6 ± 1.6	73.9 ± 1.9	73.3 ± 1.6	72.9 ± 0.8	74.6 ± 1.8
Fiber: g	4.0 ± 1.0	5.5 ± 0.6	3.6 ± 0.8	4.3 ± 0.9	3.6 ± 0.2	4.0 ± 0.5	6.2 ± 1.7	8.4 ± 0.7	3.6 ± 0.3
Calcium: mg	795 ± 218	1107 ± 90	476 ± 84	746 ± 126	496 ± 54	260 ± 47	314 ± 55	519 ± 31	237 ± 54
Phosphorus: mg	1499 ± 279	1777 ± 104	1063 ± 108	1124 ± 140	1018 ± 46	678 ± 67	911 ± 130	1374 ± 52	709 ± 79
Sodium: g	1.7 ± 0.4	2.9 ± 0.2	1.7 ± 0.2	3.0 ± 0.3	1.7 ± 0.1	0.8 ± 0.2	1.0 ± 0.2	0.9 ± 0.1	0.8 ± 0.1
Potassium: g	2.3 ± 0.3	3.4 ± 0.2	2.4 ± 0.3	3.5 ± 0.7	4.0 ± 0.3	2.7 ± 0.3	4.4 ± 0.3	6.0 ± 0.3	3.0 ± 0.6
Zinc: mg	7.8 ± 1.4	9.9 ± 0.7	7.0 ± 0.8	8.4 ± 1.3	---	---	---	---	---
Iron: Total: mg	12.9 ± 2.3	15.2 ± 0.9	11.8 ± 1.4	15.5 ± 1.6	18.4 ± 1.3	14.2 ± 2.6	20.6 ± 3.3	49.1 ± 3.3	17.8 ± 3.4
Iron: "Animal": mg	5.2 ± 0.9	6.1 ± 0.4	4.8 ± 0.8	6.2 ± 0.7	7.8 ± 1.1	1.3 ± 0.3	2.9 ± 1.9	1.5 ± 0.2	0.4 ± 0.1
Iron: "Vegetable": mg	7.7 ± 1.4	9.1 ± 0.6	7.0 ± 0.8	9.3 ± 1.0	10.6 ± 0.8	12.9 ± 1.2	17.7 ± 2.3	47.9 ± 0.2	15.9 ± 0.1
Vitamin A: ug retinol	1116 ± 390	2016 ± 257	1016 ±153	782 ± 65	579 ± 55	204 ± 33	460 ± 40	371 ± 46	337 ± 64
Thiamin: mg	1.2 ± 0.2	1.5 ± 0.1	1.2 ± 0.2	1.6 ± 0.2	0.9 ± 0.1	0.5 ± 0.1	0.9 ± 0.2	1.1 ± 0.1	0.6 ± 0.1
Riboflavin: mg	1.9 ± 0.5	2.2 ± 0.1	1.3 ± 0.2	0.9 ± 0.1	1.7 ± 0.1	0.8 ± 0.1	1.4 ± 0.3	1.6 ± 0.1	0.7 ± 0.1
Niacin: mg	14.4 ± 3.6	23.3 ± 1.6	15.6 ± 1.6	20.3 ± 2.9	14.0 ± 0.7	9.1 ± 1.1	12.0 ± 2.4	14.8 ± 0.6	10.5 ± 0.5
Ascorbic Acid: mg	11 ± 4	142 ± 17	109 ± 28	66 ± 20	98 ± 8	68 ± 11	84 ± 13	99 ± 5	73 ± 14
Folacin: ug monoglutamate	242 ± 41	246 ± 16	188 ± 35	173 ± 21	---	---	---	---	---

Table 4

Daily Nutrient Intake of Adult Women[1]

	Mexican American	White	Black	Oriental	Bolivian(H)	Chapare(L)	Oruro(L)	Cochabamba(L)	Colomi(L)
N	15	106	62	16	87	49	52	212	32
Energy: kcals	928 ± 190	1747 ± 61	1915 ± 242	1532 ± 112	1789 ± 56	1500 ± 70	1433 ± 112	2064 ± 71	1363 ± 95
Energy: kcals/kg	11.3 ± 1.0	29.4 ± 1.6	31.1 ± 4.5	28.8 ± 2.5	31.8 ± 1.2	26.9 ± 1.5	28.8 ± 2.5	37.1 ± 1.5	24.6 ± 2.5
Protein: g	43 ± 3	68 ± 3	61 ± 6	63 ± 11	65 ± 3	52 ± 3	46 ± 4	61 ± 2	51 ± 4
Protein: g/kg	0.5 ± 0.1	1.1 ± 0.1	1.0 ± 0.1	1.3 ± 0.2	1.2 ± 0.1	0.9 ± 0.1	0.8 ± 0.1	1.1 ± 0.1	0.9 ± 0.1
Protein: % energy	20.2 ± 2.1	15.9 ± 0.5	13.1 ± 0.7	16.5 ± 2.2	14.6 ± 0.3	13.9 ± 0.6	13.3 ± 0.8	11.9 ± 0.2	14.9 ± 0.7
Tryptophan: mg	568 ± 2.1	794 ± 33	656 ± 79	811 ± 125	819 ± 31	653 ± 62	487 ± 31	750 ± 31	622 ± 57
Lysine: mg	3217 ± 137	4195 ± 203	3734 ± 477	4244 ± 678	4364 ± 205	3047 ± 394	2279 ± 193	3406 ± 150	2936 ± 374
Histidine: mg	1236 ± 73	1818 ± 79	1619 ± 208	1755 ± 283	1887 ± 83	1483 ± 165	1108 ± 90	1616 ± 68	1371 ± 150
Fat: g	36 ± 5	69 ± 3	79 ± 9	47 ± 6	45 ± 3	26 ± 3	17 ± 3	24 ± 2	15 ± 2
Fat: % energy	40.6 ± 1.9	34.8 ± 0.9	34.6 ± 1.7	27.6 ± 2.3	22.3 ± 0.8	14.4 ± 1.1	12.5 ± 0.9	10.4 ± 0.7	9.5 ± 0.8
Carbohydrates: g	107 ± 36	214 ± 9	218 ± 23	214 ± 16	282 ± 9	264 ± 11	275 ± 21	378 ± 13	250 ± 15
Carbohydrates: % energy	42.9 ± 5.9	48.9 ± 1.1	49.5 ± 2.4	55.9 ± 2.9	63.5 ± 1.0	71.2 ± 1.4	77.2 ± 1.4	73.9 ± 0.8	74.2 ± 1.2
Fiber: g	0.5 ± 0.2	4.6 ± 0.3	2.9 ± 0.5	2.7 ± 0.7	3.3 ± 0.2	3.9 ± 0.2	6.2 ± 1.0	6.3 ± 0.4	3.7 ± 0.3
Calcium: mg	615 ± 86	955 ± 51	484 ± 57	488 ± 87	495 ± 32	393 ± 46	282 ± 34	398 ± 23	243 ± 32
Phosphorus: mg	772 ± 91	1226 ± 54	934 ± 108	1122 ± 107	899 ± 29	786 ± 44	724 ± 60	1091 ± 40	745 ± 49
Sodium: g	0.9 ± 0.2	2.3 ± 0.1	2.0 ± 0.2	1.9 ± 0.2	1.4 ± 0.1	1.3 ± 0.2	0.7 ± 0.1	0.8 ± 0.1	0.8 ± 0.1
Potassium: g	1.2 ± 0.3	2.6 ± 0.1	1.9 ± 0.2	2.0 ± 0.2	4.4 ± 0.3	3.0 ± 0.2	4.5 ± 0.7	4.5 ± 0.2	3.7 ± 0.5
Zinc: mg	4.2 ± 0.3	7.6 ± 0.4	5.6 ± 0.8	6.6 ± 0.6	---	---	---	---	---
Iron: Total: mg	3.6 ± 0.3	11.7 ± 0.6	9.5 ± 1.2	11.6 ± 1.0	15.5 ± 0.7	13.7 ± 0.6	17.7 ± 2.0	35.3 ± 0.1	19.6 ± 2.8
Iron: "Animal": mg	1.5 ± 0.1	4.7 ± 0.2	3.8 ± 0.5	4.6 ± 0.4	3.9 ± 0.3	1.6 ± 0.5	0.4 ± 0.1	1.4 ± 0.3	0.6 ± 0.1
Iron: "Vegetable": mg	2.1 ± 0.1	7.0 ± 0.4	5.7 ± 0.7	7.0 ± 0.6	11.6 ± 0.9	12.1 ± 0.7	17.3 ± 1.1	33.9 ± 0.1	18.6 ± 2.9
Vitamin A: ug retinol	661 ± 182	1891 ± 142	758 ± 119	1320 ± 335	566 ± 37	264 ± 26	370 ± 75	521 ± 96	271 ± 36
Thiamin: mg	0.4 ± 0.1	1.1 ± 0.1	1.0 ± 0.1	1.4 ± 0.2	0.7 ± 0.1	0.7 ± 0.1	0.6 ± 0.1	0.8 ± 0.1	0.6 ± 0.1
Riboflavin: mg	1.1 ± 0.2	1.5 ± 0.1	1.2 ± 0.1	1.0 ± 0.1	1.4 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.4 ± 0.1	0.8 ± 0.1
Niacin: mg	7.3 ± 0.9	15.5 ± 0.8	14.1 ± 2.0	18.3 ± 3.5	11.7 ± 0.5	10.6 ± 0.8	11.6 ± 1.3	11.7 ± 0.5	10.6 ± 0.9
Ascorbic Acid: mg	9 ± 3	117 ± 10	67 ± 14	91 ± 13	89 ± 6	68 ± 9	72 ± 12	82 ± 4	65 ± 8
Folacin: ug monoglutamate	69 ± 5	178 ± 10	153 ± 24	155 ± 23	---	---	---	---	---

Table 5
Concentration of Hormones in Human Plasma[1]

TABLE 5

Concentration of hormones in human plasma[1]

Variable	Mexican American	White	Black	Oriental	Bolivian Professionals	Chapare	Oruro	Cochabamba	Colomi
N	30	163	109	29	125	78	95	390	51
Fat: % energy	40.8 ± 2.0	35.6 ± 0.8	33.7 ± 1.5	31.6 ± 1.9	22.4 ± 0.7	13.9 ± 0.9	12.2 ± 0.9	10.2 ± 0.4	9.8 ± 0.7
Altitude: m	<250	<250	<250	<250	2557	<250	3706	2557	3200
Insulin: uU/ml	15.7 ± 1.6	13.1 ± 0.7	23.4 ± 2.1	12.2 ± 1.4	17.4 ± 1.1	19.4 ± 1.9	19.4 ± 1.4	15.8 ± 0.8	19.4 ± 1.7
Glucagon: ng/dl	126 ± 16	153 ± 8	117 ± 7	136 ± 16	128 ± 6	134 ± 10	121 ± 7	139 ± 4	172 ± 15
T3: ng/dl	156 ± 5	132 ± 3	135 ± 3	132 ± 6	140 ± 4	141 ± 5	139 ± 6	148 ± 2	162 ± 6
T3 uptake	38.9 ± 1.0	39.6 ± 0.5	41.3 ± 0.7	47.0 ± 0.9	41.0 ± 0.4	38.7 ± 0.8	42.4 ± 0.6	36.4 ± 0.3	34.9 ± 1.0
RT3: pg/ml	---	205 ± 6	237 ± 8	---	---	---	---	---	---
T4: ug/dl	9.5 ± 0.6	9.7 ± 0.2	9.2 ± 0.2	8.7 ± 0.4	7.7 ± 0.2	9.3 ± 0.4	9.3 ± 0.2	8.7 ± 0.1	9.8 ± 0.5
T4/T3: ratio	6.2 ± 0.5	8.1 ± 0.5	8.0 ± 0.5	6.9 ± 0.4	5.9 ± 0.3	7.1 ± 0.3	7.7 ± 0.4	6.3 ± 0.1	6.4 ± 0.4
TSH: ng/ml	5.1 ± 0.3	4.9 ± 0.4	3.5 ± 0.2	4.2 ± 0.3	4.0 ± 0.2	3.8 ± 0.2	3.7 ± 0.2	3.1 ± 0.1	3.9 ± 0.2
Parathyroid Hormone (PTH): pmol/l	---	1.05 ± 0.05	0.90 ± 0.07	---	---	---	---	---	---
Corticosterone: ug/dl	1.27 ± 0.08	1.47 ± 0.05	1.68 ± 0.08	2.07 ± 0.10	2.10 ± 0.13	1.10 ± 0.06	1.24 ± 0.05	1.39 ± 0.03	0.94 ± 0.06
Cortisol: ug/dl	20.4 ± 1.7	18.9 ± 0.7	21.1 ± 1.1	16.6 ± 1.7	11.4 ± 0.3	11.3 ± 0.8	11.9 ± 0.4	13.3 ± 0.4	14.4 ± 0.8
Cortisol/Corticosterone: ratio	15.8 ± 0.8	12.7 ± 0.6	13.6 ± 0.5	7.8 ± 0.4	6.4 ± 0.3	9.7 ± 0.3	10.3 ± 0.4	12.6 ± 0.5	15.5 ± 0.5
ACTH: ng/ml	74 ± 8	37 ± 3	63 ± 5	55 ± 11	38 ± 4	30 ± 6	49 ± 8	78 ± 5	78 ± 6
DOPA: ng/ml	---	1.4 ± 0.1	2.2 ± 0.2	---	---	---	---	---	---
Norepinephrine (NE): pg/ml	---	354 ± 22	479 ± 23	---	---	---	---	---	---
IgG: mg/dl (=NE)	1242 ± 57	1161 ± 25	1635 ± 40	1305 ± 51	1473 ± 32	1957 ± 56	1649 ± 45	1593 ± 18	2039 ± 57
IgA: mg/dl (=epinephrine)	179 ± 22	204 ± 9	233 ± 10	257 ± 17	253 ± 9	242 ± 9	270 ± 9	288 ± 6	266 ± 14
C3: mg/dl (=ADH)	107 ± 5	122 ± 3	142 ± 5	109 ± 5	136 ± 3	142 ± 4	134 ± 3	119 ± 1	161 ± 6
C4: mg/dl (=Calcitonin)	18 ± 1	27 ± 1	36 ± 2	22 ± 2	29 ± 1	25 ± 1	27 ± 1	25 ± 1	24 ± 4
Prolactin: ng/ml; male	14.1 ± 2.0	18.0 ± 2.0	18.3 ± 2.0	21.4 ± 2.6	19.7 ± 2.0	22.9 ± 4.7	34.4 ± 16.2	22.2 ± 4.3	17.1 ± 2.6
female	12.5 ± 1.3	19.6 ± 1.0	30.7 ± 3.5	24.9 ± 3.1	24.4 ± 1.8	91.4 ± 18.8	48.7 ± 11.6	21.2 ± 3.4	103.5 ± 31.2
Growth hormone: ng/ml; male	1.3 ± 0.3	1.7 ± 0.5	2.8 ± 0.8	0.3 ± 0.1	0.9 ± 0.2	3.5 ± 1.0	2.4 ± 0.8	2.6 ± 0.5	3.6 ± 0.7
female	2.9 ± 1.1	7.0 ± 1.0	4.7 ± 1.0	5.0 ± 1.1	2.7 ± 0.5	6.5 ± 1.1	4.6 ± 1.3	2.9 ± 0.4	7.5 ± 0.8
Testosterone: pg/ml; male	4.6 ± 0.2	5.9 ± 0.3	5.7 ± 0.3	4.9 ± 0.3	4.8 ± 0.5	3.9 ± 0.2	3.7 ± 0.5	1.5 ± 0.3	---
female	0.3 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.2 ± 0.1	0.4 ± 0.1	0.3 ± 0.1	0.2 ± 0.1	0.2 ± 0.1	---
Estrone (E1): pg/ml; male	19 ± 2	38 ± 2	39 ± 2	37 ± 6	66 ± 7	---	---	---	---
female	22 ± 5	68 ± 2	50 ± 3	79 ± 5	71 ± 5	---	---	---	---
Estradiol (E2): pg/ml; male	10 ± 3	16 ± 2	19 ± 3	15 ± 2	12 ± 2	15 ± 2	3 ± 1	---	---
female	5 ± 2	50 ± 5	30 ± 6	52 ± 7	43 ± 6	44 ± 7	25 ± 5	---	---
Estriol (E3): ng/dl; male	12 ± 2	30 ± 3	17 ± 4	31 ± 5	80 ± 8	41 ± 8	6 ± 2	44 ± 7	52 ± 8
female	4 ± 1	16 ± 2	12 ± 2	9 ± 3	62 ± 4	16 ± 5	2 ± 1	33 ± 5	50 ± 8
Progesterone: ng/dl; male	30 ± 4	24 ± 3	26 ± 3	14 ± 4	107 ± 3	130 ± 29	105 ± 11	65 ± 10	129 ± 11
female	27 ± 7	160 ± 24	101 ± 19	17 ± 6	201 ± 32	143 ± 31	153 ± 29	110 ± 20	150 ± 19
Follicle Stimulating Hormone: mIU/ml; male	7.7 ± 2.4	5.7 ± 1.3	5.5 ± 1.0	3.7 ± 0.8	7.8 ± 1.3	14.4 ± 1.3	12.4 ± 3.7	7.5 ± 2.0	---
female	4.3 ± 1.0	8.5 ± 1.0	11.5 ± 2.0	7.0 ± 2.4	28.7 ± 3.5	21.8 ± 2.3	25.0 ± 4.5	19.8 ± 4.3	---

[1]Results are means ± SE.

Table 6
Plasma Concentrations of Biochemical Constituents[1]

TABLE 6

Plasma concentrations of biochemical constituents[1]

Variable		Mexican American	White	Black	Oriental	Bolivian Professionals	Chapare	Oruro	Cochabamba	Colcal
N		30	163	109	29	125	78	95	390	51
Sodium: mE/L		135 ± 1	148 ± 1	147 ± 2	156 ± 2	140 ± 1	139 ± 1	140 ± 1	150 ± 1	146 ± 1
Potassium: mE/L		5.8 ± 0.1	4.6 ± 0.1	4.4 ± 0.1	4.7 ± 0.1	5.2 ± 0.2	6.6 ± 0.3	5.0 ± 0.1	4.8 ± 0.1	4.8 ± 0.2
Calcium: mg/dl		8.4 ± 0.2	9.2 ± 0.1	9.3 ± 0.2	10.5 ± 0.2	10.1 ± 0.2	10.1 ± 0.2	10.4 ± 0.2	12.2 ± 0.1	10.9 ± 0.2
Zinc: ug/dl		---	140 ± 3	131 ± 3	---	---	---	---	---	---
Iron: ug/dl;	male	127 ± 10	123 ± 6	113 ± 6	133 ± 10	133 ± 7	93 ± 6	135 ± 7	139 ± 4	122 ± 14
	female	75 ± 14	111 ± 5	93 ± 6	112 ± 14	109 ± 5	82 ± 5	101 ± 5	117 ± 3	101 ± 8
Transferrin: mg/dl		342 ± 12	361 ± 7	353 ± 12	332 ± 13	347 ± 6	397 ± 13	345 ± 7	354 ± 3	359 ± 11
Saturation of Transferrin: %;	male	30 ± 2	28 ± 2	29 ± 1	33 ± 2	35 ± 2	22 ± 2	33 ± 2	33 ± 1	29 ± 3
	female	17 ± 3	24 ± 1	20 ± 2	27 ± 3	26 ± 1	17 ± 1	23 ± 1	27 ± 1	23 ± 2
Ferritin: ng/ml;	male	61 ± 7	97 ± 10	137 ± 18	148 ± 34	150 ± 20	48 ± 10	132 ± 14	165 ± 13	511 ± 104
	female	21 ± 5	26 ± 3	32 ± 4	55 ± 15	37 ± 4	30 ± 5	64 ± 10	89 ± 6	180 ± 37
Folacin: ng/ml		7.4 ± 0.9	8.6 ± 0.4	5.9 ± 0.3	7.8 ± 0.6	6.5 ± 0.2	5.9 ± 0.3	6.2 ± 0.3	8.0 ± 0.1	5.3 ± 0.3
Vitamin B12: pg/ml		---	479 ± 28	513 ± 20	---	---	---	---	---	---
Histidine: mg/dl		16.1 ± 0.3	17.5 ± 0.2	17.3 ± 0.3	17.9 ± 0.4	18.8 ± 0.2	20.7 ± 0.4	20.4 ± 0.3	19.0 ± 0.1	17.6 ± 0.3
Tryptophan: ug/ml;	male	16.7 ± 0.7	17.3 ± 0.5	15.4 ± 0.5	16.8 ± 0.6	17.2 ± 0.5	14.0 ± 0.4	15.8 ± 0.5	15.0 ± 0.6	15.3 ± 0.7
	female	15.9 ± 0.6	14.6 ± 0.2	13.7 ± 0.5	14.3 ± 0.5	15.2 ± 0.2	12.6 ± 0.4	13.3 ± 0.5	13.6 ± 0.4	12.3 ± 0.6
Serotonin: ng/ml		11.7 ± 2.7	21.4 ± 1.1	22.6 ± 1.9	14.0 ± 1.3	28.1 ± 3.2	52.6 ± 9.1	27.3 ± 2.9	22.1 ± 2.8	20.4 ± 2.7
IgA: mg/dl		179 ± 22	204 ± 9	233 ± 10	245 ± 10	255 ± 9	242 ± 9	270 ± 9	288 ± 6	266 ± 14
IgG: mg/dl		1242 ± 57	1161 ± 25	1635 ± 40	1305 ± 51	1473 ± 32	1957 ± 56	1649 ± 45	1593 ± 18	2039 ± 57
IgM: mg/dl;	male	160 ± 16	135 ± 13	136 ± 11	116 ± 10	168 ± 11	183 ± 10	180 ± 12	153 ± 6	188 ± 17
	female	191 ± 19	195 ± 9	184 ± 11	131 ± 9	207 ± 9	220 ± 12	212 ± 11	185 ± 6	211 ± 12
C3: mg/dl		107 ± 5	122 ± 3	142 ± 5	109 ± 5	136 ± 3	142 ± 4	134 ± 3	119 ± 1	161 ± 6
C4: mg/dl		18 ± 1	27 ± 1	36 ± 2	22 ± 2	29 ± 1	25 ± 1	27 ± 1	25 ± 1	24 ± 4
Total Protein: g/dl		8.1 ± 0.1	7.4 ± 0.1	7.8 ± 0.1	7.4 ± 0.1	7.8 ± 0.1	8.4 ± 0.1	7.9 ± 0.1	7.8 ± 0.1	8.6 ± 0.2
Albumin: g/dl		5.5 ± 0.1	5.0 ± 0.1	5.0 ± 0.1	5.1 ± 0.1	5.0 ± 0.1	4.8 ± 0.1	5.0 ± 0.1	4.8 ± 0.1	4.7 ± 0.1
Globulins: g/dl		2.5 ± 0.1	2.4 ± 0.1	2.8 ± 0.1	2.3 ± 0.1	2.8 ± 0.1	3.6 ± 0.1	2.9 ± 0.1	3.0 ± 0.1	3.9 ± 2.0
Cholesterol: mg/dl		160 ± 6	202 ± 3	182 ± 5	205 ± 8	173 ± 3	144 ± 5	156 ± 5	147 ± 2	149 ± 6
Phospholipids: mg Pl/dl		5.8 ± 0.3	7.2 ± 0.2	7.0 ± 0.2	7.3 ± 0.4	7.7 ± 0.1	6.6 ± 0.3	6.5 ± 0.3	7.3 ± 0.2	5.7 ± 0.4
Triglycerides: mg/dl		115 ± 10	80 ± 3	88 ± 5	129 ± 21	100 ± 4	106 ± 6	110 ± 6	92 ± 2	105 ± 6
Retinol binding protein: mg/dl;	male	6.2 ± 0.3	6.8 ± 0.3	6.5 ± 0.2	6.8 ± 0.3	6.6 ± 0.3	5.5 ± 0.2	5.3 ± 0.4	6.5 ± 0.2	6.3 ± 0.3
	female	4.6 ± 0.3	5.6 ± 0.2	5.8 ± 0.3	4.9 ± 0.4	6.1 ± 0.4	4.4 ± 0.3	4.7 ± 0.2	5.1 ± 0.4	5.2 ± 0.3
Plasma Renin Activity(PRA): ng/ml/hr		---	3.16 ± 0.26	2.49 ± 0.25	2.81 ± 0.24	---	---	---	---	---
Angiotensin I(AGI): ng/ml		---	0.65 ± 0.02	0.61 ± 0.02	0.60 ± 0.01	---	---	---	---	---

[1]Results are means ± SE for both sexes combined unless stated otherwise.

Table 7
Hematological and Biological Effects of Feeding Young Male Rats for Two Weeks Diets Defficient in a Single Amino Acid[1]

Variable	AA[2]	AA-tryptophan (0)	AA-tryptophan (0) + niacin	AA-Leucine (0)	AA-Lysine (0)	AA-Histidine (0)
N	25	25	25	25	25	25
Initial wt: g	326 ± 4	317 ± 5	317 ± 5	320 ± 4	318 ± 4	322 ± 4
Wt at killing: g	367 ± 5	260 ± 3[3]	260 ± 3[3]	260 ± 3[3]	275 ± 3[3]	267 ± 3[3]
Hemoglobin: g/dl	15.6 ± 0.1	16.5 ± 0.1[3]	16.7 ± 0.1[3]	16.3 ± 0.1[3]	15.9 ± 0.1	15.9 ± 0.1
Serotonin: ng/ml	361 ± 46	291 ± 48[3]	321 ± 50	412 ± 65	400 ± 50	350 ± 45[3]
Tryptophan: ug/ml	31.3 ± 0.8	25.9 ± 0.6[3]	28.3 ± 0.6[3]	30.0 ± 0.8	25.6 ± 0.7[3]	26.8 ± 0.8[3]
Glucagon: pg/ml	86.9 ± 3.6	108.0 ± 6.9[3]	87.0 ± 4.3	89.0 ± 5.0	100.3 ± 6.7[3]	87.2 ± 4.2
Insulin: uU/ml	21.8 ± 2.6	10.8 ± 0.7[1]	8.8 ± 0.6[3]	8.0 ± 0.6[3]	11.1 ± 1.7[3]	11.1 ± 0.8[3]
ACTH: pg/ml	450 ± 29	590 ± 30[3]	570 ± 29[3]	505 ± 28	570 ± 29[3]	550 ± 30[3]
Corticosterone: ug/dl	43.4 ± 2.5	37.9 ± 3.8	40.1 ± 3.8	29.4 ± 4.0[3]	41.8 ± 3.4	39.6 ± 3.4
Vitamin A: ug/dl	42.6 ± 1.3	25.5 ± 1.4[3]	30.1 ± 1.8[3]	19.0 ± 1.2[3]	34.2 ± 1.3	21.7 ± 1.3[3]
Liver ATPase: umol Pi/mg protein/hr	0.76 ± 0.02	0.77 ± 0.02	0.74 ± 0.02	0.63 ± 0.02[3]	0.64 ± 0.03[3]	0.76 ± 0.03
Erythrocyte Naa: mE/L	3.3 ± 0.2	2.6 ± 0.2[3]	2.3 ± 0.2[3]	2.5 ± 0.2[3]	2.3 ± 0.2[3]	2.1 ± 0.2[3]
Erythrocyte Ka: mE/L	76.0 ± 1.7	79.6 ± 1.5[3]	81.7 ± 1.3[3]	85.9 ± 2.0[3]	80.8 ± 1.5[3]	79.3 ± 1.9[3]

FIGURE 1

Overall Hypothesis

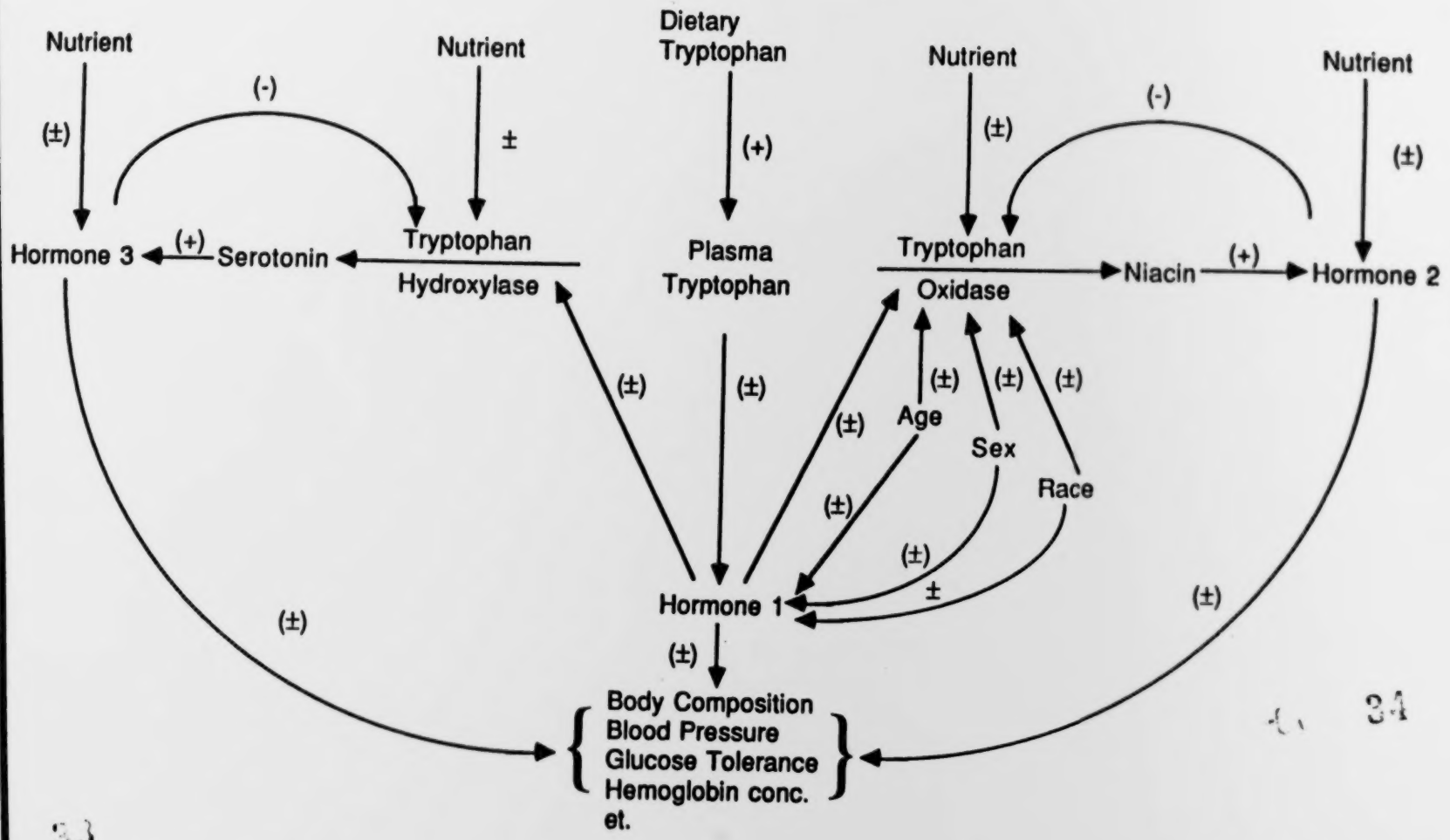
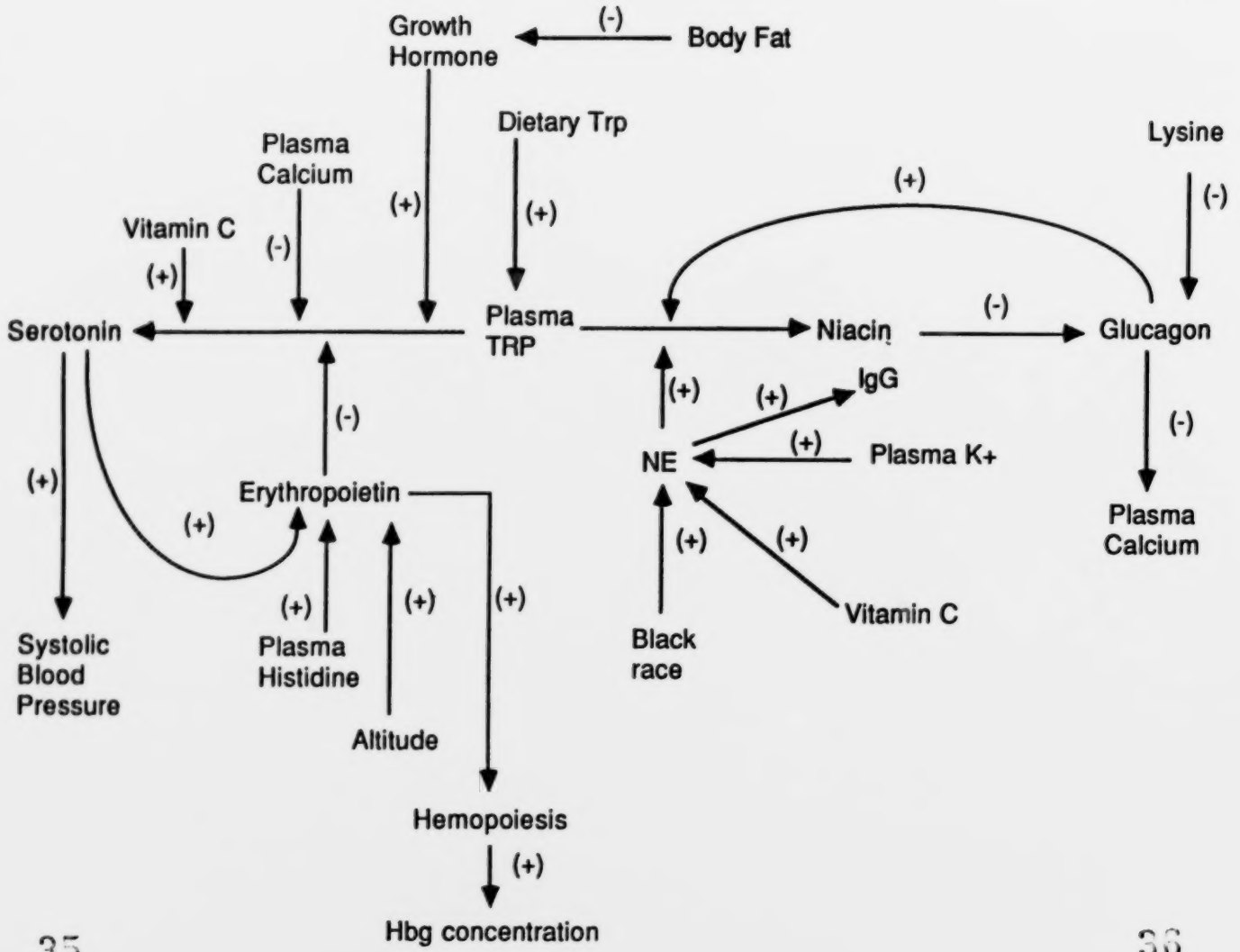


FIGURE 2

The Metabolism of Tryptophan



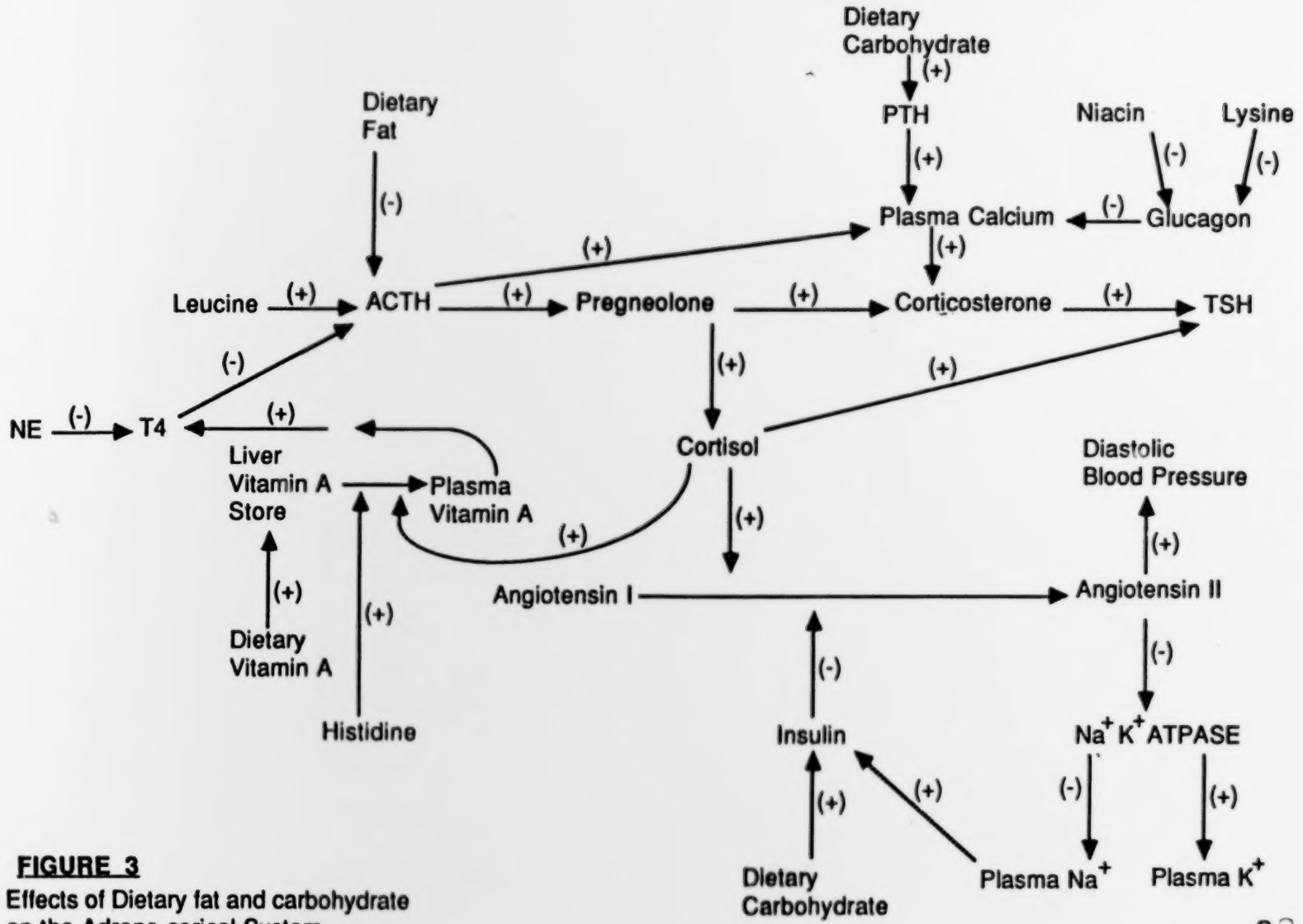


FIGURE 3

Effects of Dietary fat and carbohydrate on the Adreno-corical System

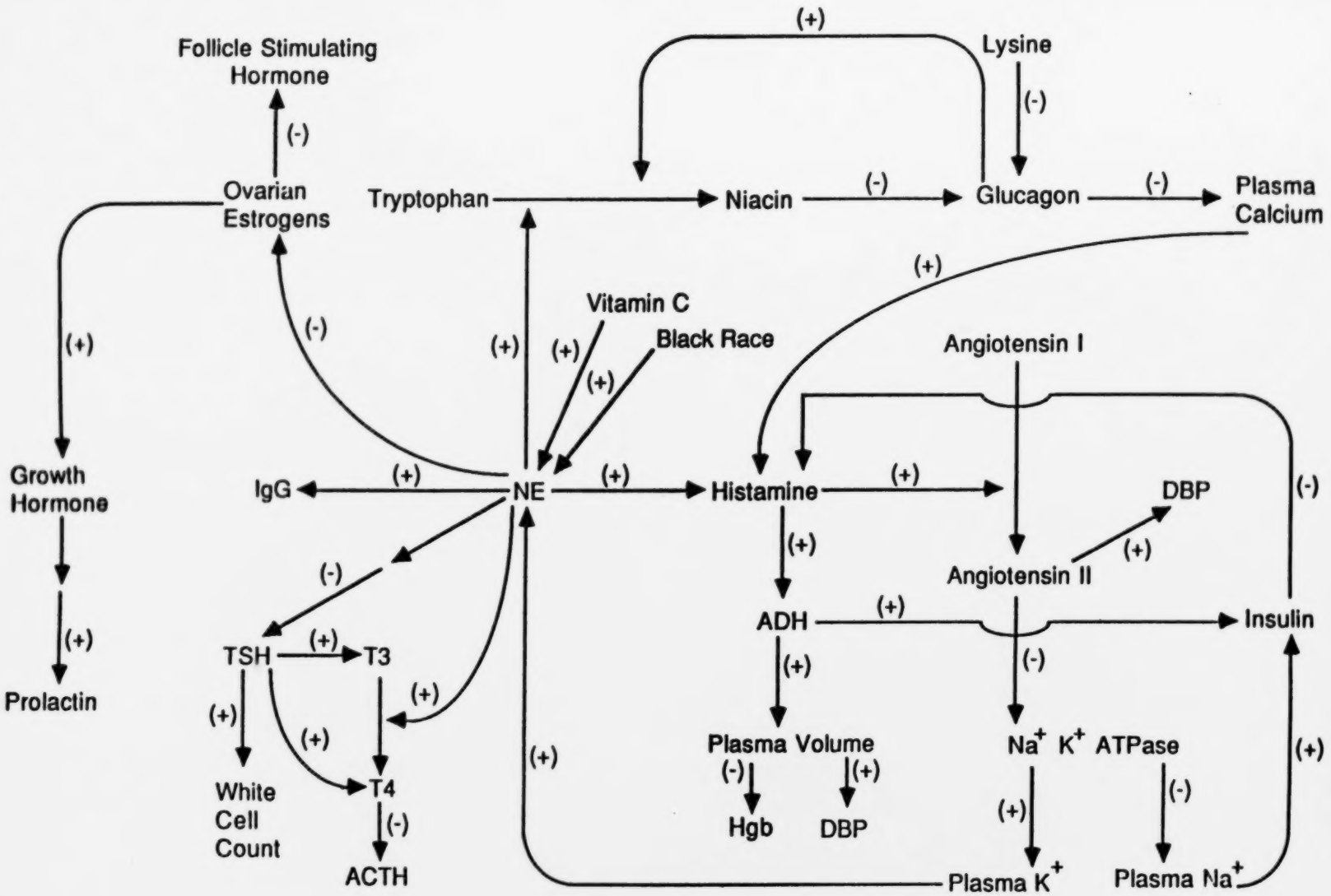


FIGURE 4

The Metabolic Effects of Norepinephrine/Epinephrine

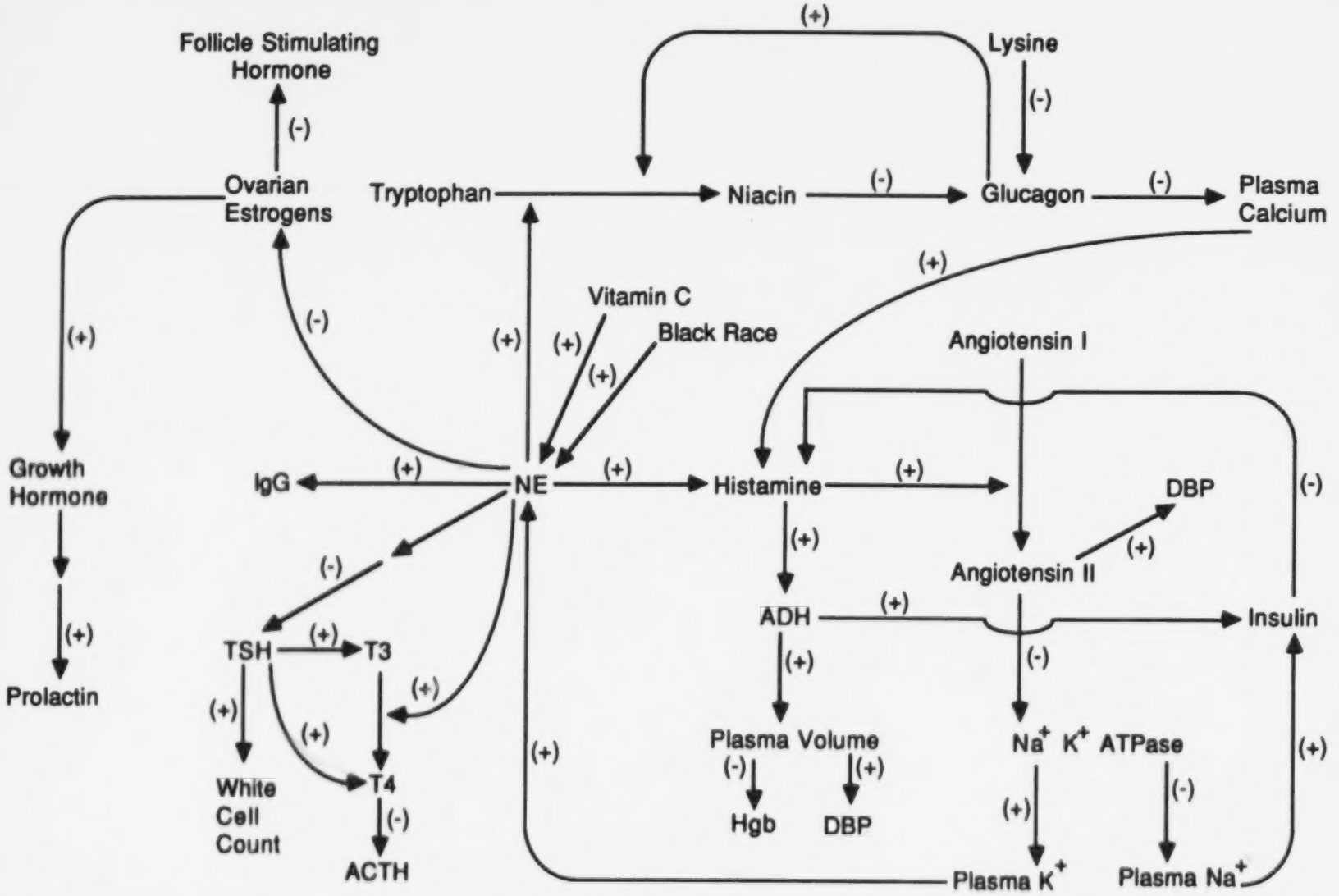


FIGURE 5

The Metabolic Effects of Norepinephrine/Epinephrine

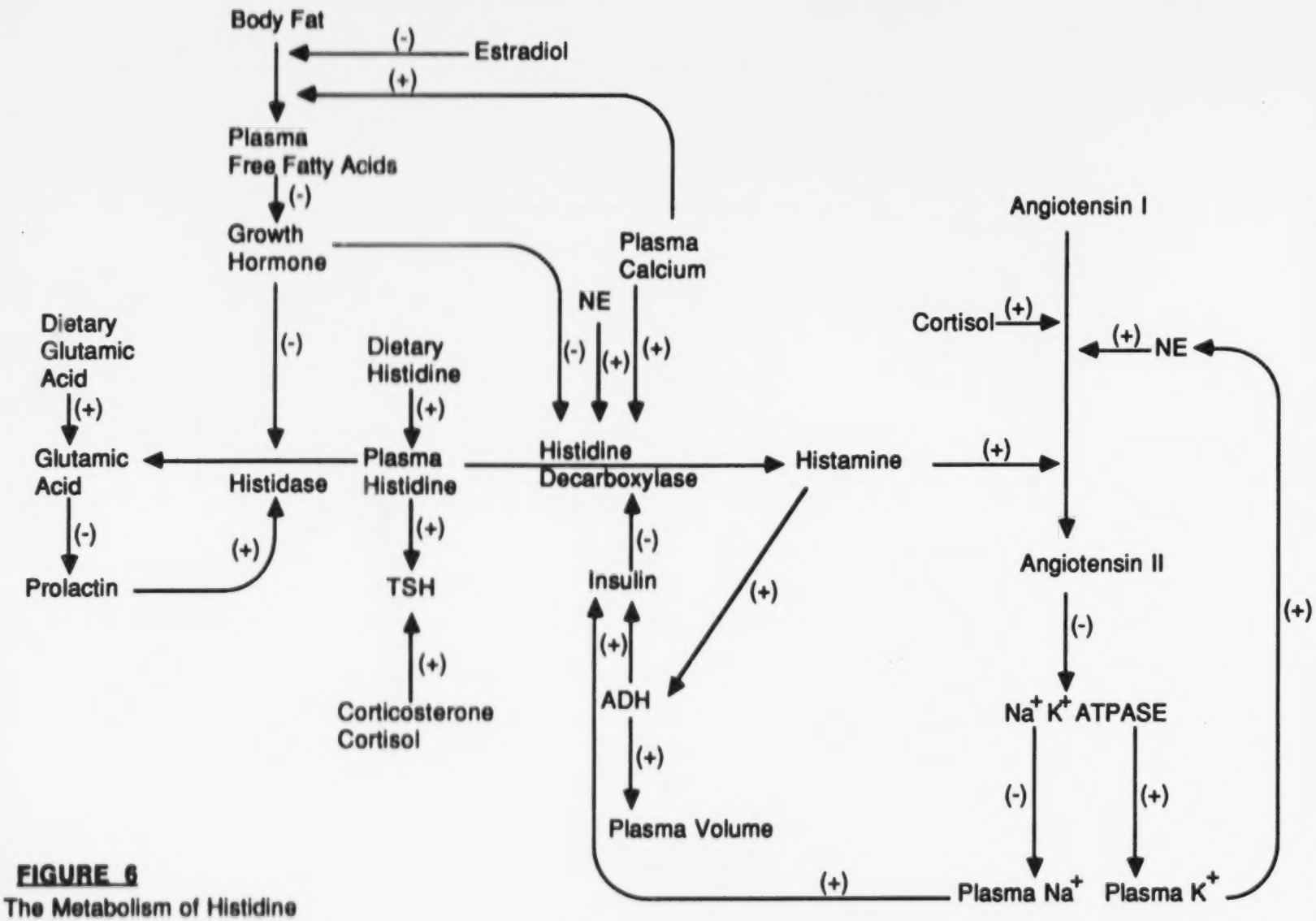


FIGURE 6
The Metabolism of Histidine

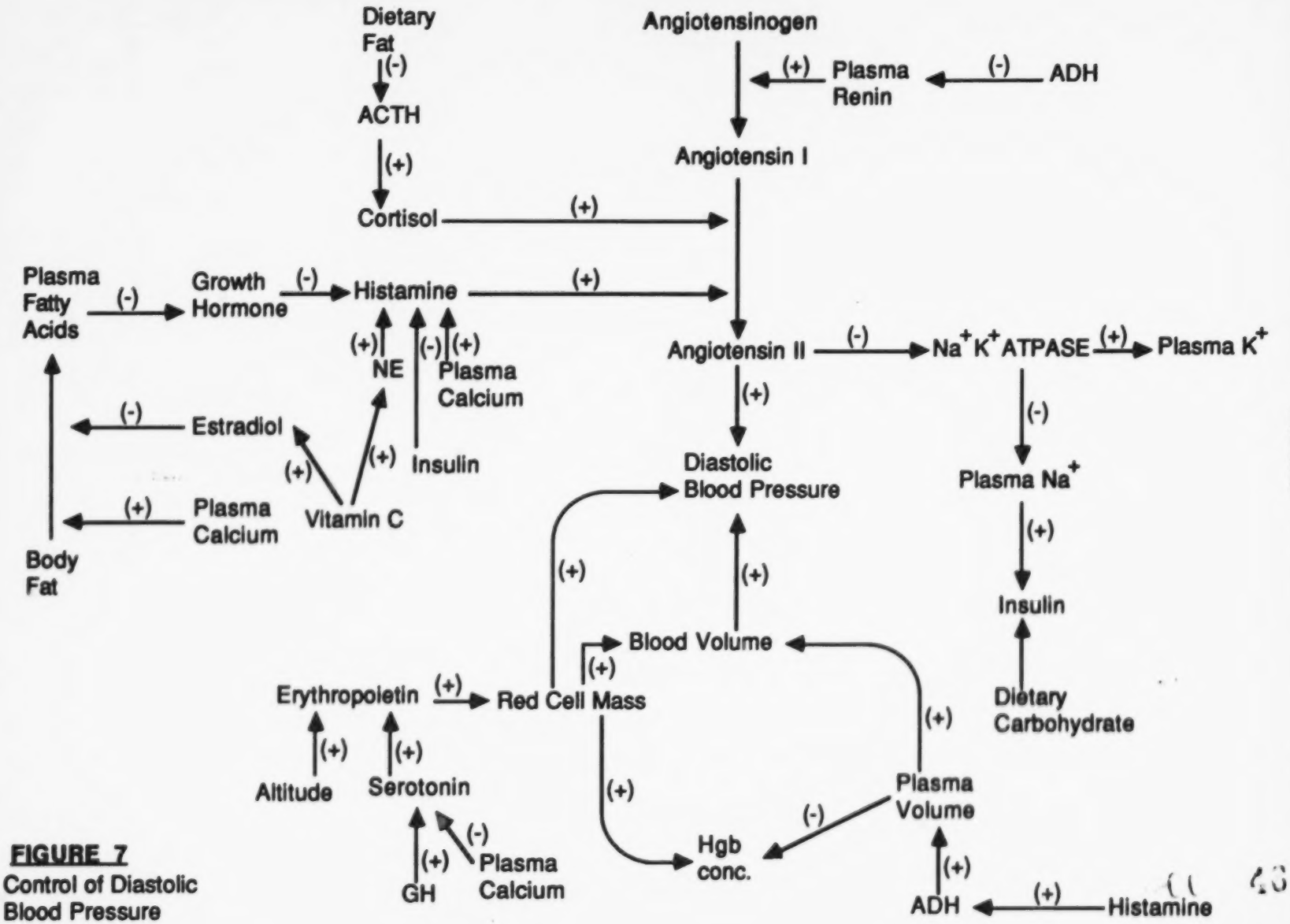


FIGURE 7
Control of Diastolic Blood Pressure

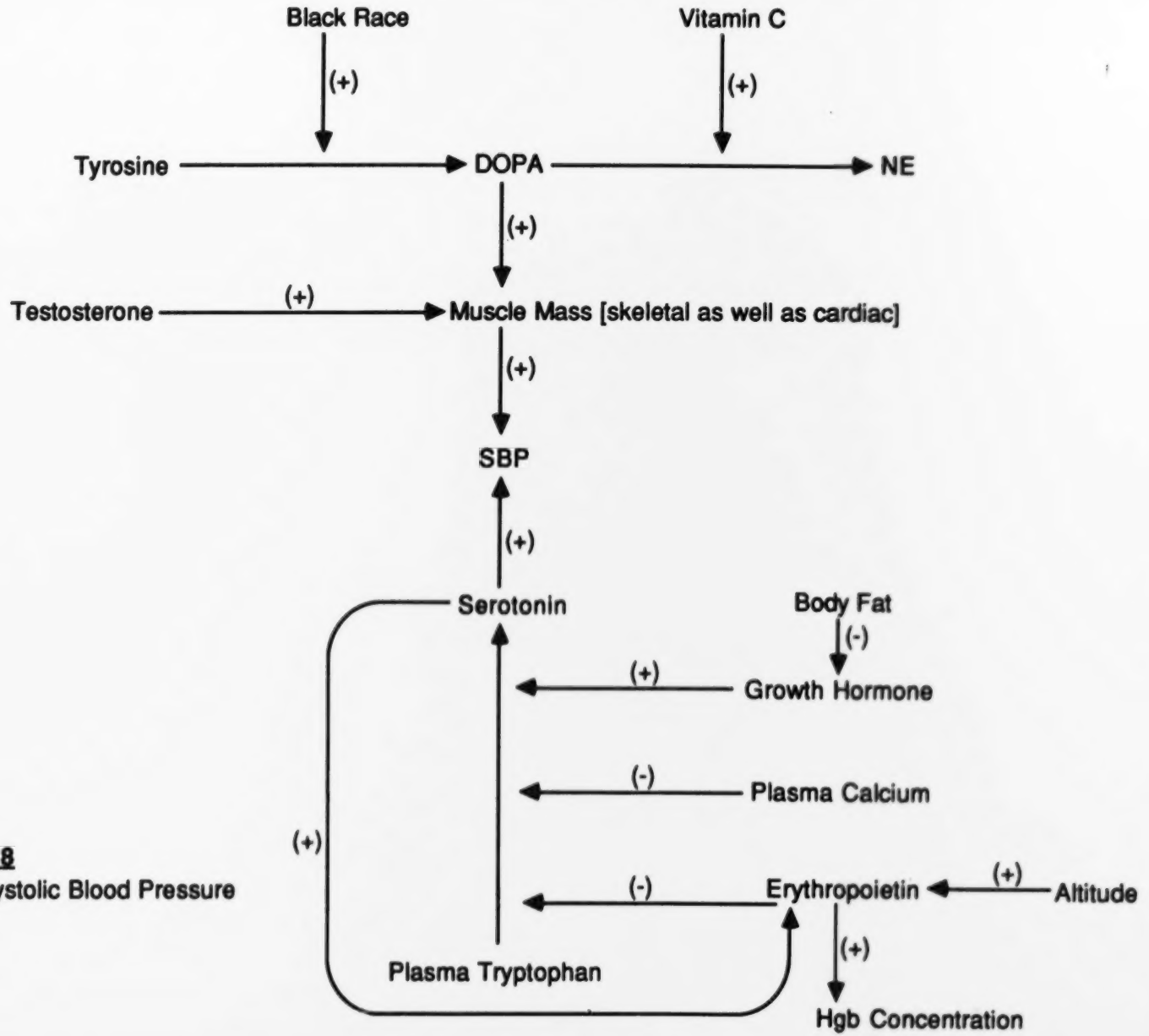


FIGURE 8
Control of Systolic Blood Pressure

DIETARY PATTERNS OF BLACKS AND OTHER MINORITIES IN THE UNITED STATES: IMPLICATIONS FOR HYPERTENSION PREVENTION AND TREATMENT

Shiriki K. Kumanyika
Department of Epidemiology
Johns Hopkins University
School of Hygiene and Public Health
Baltimore, MD

Introduction

Dietary changes are obvious concomitants of modernization and cultural change and of the associated epidemiologic transitions in disease patterns (1,2). Although causes of chronic diseases are difficult to pinpoint, plausible mechanisms involving dietary factors have been postulated for cardiovascular diseases and cancers, and dietary modifications have been recommended as measures for primary or secondary prevention (3). Hypertension is an important area of interest in this respect. Possible mechanisms for the influence of nutrients on blood pressure discussed in the 1988 Surgeon General's Report on Nutrition and Health (3) are shown in Table 1.

Hypertension affects up to 58 million U. S. adults, increasing their risks of heart and renal diseases and stroke (3,4). Side effects lower the overall utility of drug therapies for hypertension. Dietary modification, presumed to be low risk, is an attractive alternative or adjunct therapy.

This paper highlights aspects of the dietary patterns of black and other minorities that may be relevant to hypertension prevention and control. Diet affects hypertension, and dietary patterns differ by race/ethnicity. Thus, racial/ethnic differences in patterns of hypertension may be diet-related. Black Americans and several other minority groups have excess hypertension in comparison with whites (5-7). Cardiovascular and cerebrovascular diseases are major causes of death in U. S. minority groups, even where these diseases are in lower prevalence than in whites (5,8).

Conceptual Issues

This discussion focuses on the factors in Table 2. The basis for each definition is given in the table footnotes. Overweight, rather than caloric intake per se, is used as a proxy for chronic consumption of excess calories, because knowledge of energy expenditure is needed in order to determine the level of caloric intake that constitutes an excess. The associations of obesity, sodium intake and alcohol intake with hypertension are generally accepted, particularly as they relate to hypertension treatment. Debates about the roles of sodium, obesity, and alcohol in hypertension etiology and about the effects of potassium, calcium, and other dietary factors on blood pressure continue (4).

In specifying chronic disease risk factors, excess or low intakes are estimated in relation to the intakes of comparison populations with low levels of hypertension. Such risk factor levels do not reflect precisely measured physiologic needs. Ideally, intakes described as low or high should have some validity for physiologic processes or thresholds. However, definitions of nutrient intake range that are harmful or protective in chronic disease processes do not necessarily overlap the ranges defined for nutritional adequacy. Nor will the physiologic mechanisms involved necessarily relate to those associated with classic deficiency or toxicity syndromes (11).

In cross-cultural comparisons of disease or risk factor prevalence, the term "excess" also refers to excess risk: higher than average rates, using rates

for whites or for the general population to represent the average (5). This excess risk concept is useful in identifying high priority target populations for nutritional interventions. However, it can be misleading as to absolute risk. For example, a lower than average risk is not necessarily a low risk if the average level of risk is high (i.e., if a large proportion of the population is affected).

In general, cross-cultural comparisons of diet-related disease risks should be interpreted with caution. Genetic or environmental factors can modify dietary effects on disease processes. For example, it has been proposed that blacks are more sensitive than whites to a physiologic excess of sodium (12). If this is true, the risk associated with a given level of sodium intake may be greater for blacks than whites. Or, if nutrient combinations have more influence on blood pressure levels than single nutrient actions (sodium and potassium or sodium and calcium rather than sodium alone, for example), multiple aspects of diet must be examined simultaneously if the cross cultural comparison is to be informative.

The American Diet

Table 3 shows selected average nutrient intakes in the American diet. Among adults, the macronutrient content (percent of total calories) is about 16-20 percent protein, 36-37 percent fat, and 45-46 percent carbohydrate. Calcium intakes of women average less than the Recommended Dietary Allowances. Taking discretionary salt use into account, sodium intakes probably exceed safe levels for both men and women. Potassium intakes are within the recommended ranges. The data in Table 3, from a 1985 survey of children and adults aged 1-5 and 19-50 years, respectively, are similar to data from the 1976-80 NHANES survey for the U. S. population aged 1 through 74 years (15).

National nutrition surveys for 1977 and 1985 show recent shifts in the macronutrient content of the U. S. diet (16). However, the changes are small relative to changes that occur over time or with increasing industrialization. Relative to diets in the early 1900's or to diets in less industrialized nations, current U. S. diets a) are more varied and include more processed foods, b) are higher in calories and simple carbohydrates and lower in complex carbohydrates, c) are higher in animal protein and lower in vegetable protein, d) are higher in both saturated and unsaturated fats, e) are higher in sodium and lower in potassium, f) are higher in phosphorous, and g) include more dairy products (17, 18). Changes in individual nutrient intakes with upward mobility are of a similar nature. As disposable income increases, consumption of animal protein, fat, and dairy products increases and carbohydrate intake decreases (19). The tendency towards an increasingly atherogenic diet may be particularly strong in men (20).

A dietary pattern such as the one in Table 3 is thought to be generally harmful, protecting against nutritional deficiencies but predisposing to Western diseases and their sequelae (1-3). Thus, racial/ethnic groups with origins in less westernized cultures might be expected to have relatively more favorable dietary patterns from a chronic disease perspective. However, since the traditional diets of some minority populations include very high sodium foods (21) (see Table 4, for example), a higher than average risk of hypertension is implied (and has been observed (5)) for these populations.

Dietary Patterns of Minority Groups

U. S. minority groups comprise racially and ethnically heterogeneous subpopulations with diverse geographical and cultural origins (23, 24). Socioeconomic characteristics also differ greatly among and within minority groups. However, on average, disproportionate numbers of minority group individuals live in poverty (23, 25). This is true even for Asian American populations, whose median income is higher than that of U. S. whites (24).

Detailed accounts of various aspects of the diets of U. S. minorities have been published elsewhere (21, 22, 25, 26, 27). The following summaries highlight factors of potential relevance to hypertension.

Black Americans

About 97 percent of U. S. blacks are native born (28). The predominant cultural influence in the black American diet is Southern, although, historically, the cooking practices of black slaves influenced Southern eating patterns (29). Black

American diets are similar in structure and content to those of the general population (21, 26, 30, 31), particularly when region and socioeconomic status are held constant. However, many blacks retain preferences for food choices and cooking methods that were shaped by conditions of slavery or sharecropping (21). Many black cultural foods are high in saturated fat and sodium. Fried, smothered and barbecued meats, hot sauce, ham hocks, and salt pork are characteristic of "soul food". Consumption of dark green leafy vegetables, cruciferous vegetables, and use of pork and chicken are high in comparison to whites (21, 25, 26, 30-32). Some evidence suggests higher than average table salt use among blacks (33). Dairy product use among blacks is limited and is different from the pattern in whites. Blacks consume more buttermilk than whites for example (15, 34).

A subpopulation of black Americans is of Caribbean origin. Caribbean diets emphasize rice and other starchy vegetables, legumes, seasoned meat mixtures, and salted fish. Cultural influences include Spanish, French, Dutch, Chinese and Amerindian (21, 35).

Hispanic Americans

About two-thirds of Hispanics are Mexican Americans residing in the West or Southwest (23). The other large Hispanic subgroups are Puerto Ricans and Cuban Americans. However, in some parts of the United States, immigrants from Central America comprise a large percentage of the Hispanic population (e.g., in the District of Columbia (36)). In the 1980 U. S. census data, 71 percent of Hispanics were native born (28).

Traditional Mexican American and Puerto Rican diets have carbohydrate staples: tortillas or rice, respectively. Consumption of leafy green vegetables is lower and consumption of vegetable protein higher than in typical U. S. diets. Dairy product consumption is also low compared to that of non-Hispanic whites. Sausages and some sauces in Mexican American and Puerto Rican diets are high in sodium (21, 25, 26). Table salt consumption may be higher than average among Mexican Americans, compared to whites living in the same geographic area (33).

Asian/Pacific Americans

Asian/Pacific Americans include persons with origins in China, Japan, Korea, the Philippines, Vietnam, Cambodia, Laos, Thailand, Bangladesh, Sri Lanka, Burma, and Pacific Islands such as Hawaii, Guam, Samoa, Tonga, and Fiji (23). The overall proportion of Asian/Pacific Americans who were foreign born was 70 percent in the 1980 census (28); however this varies markedly in different subgroups. Asian/Pacific Americans are the fastest growing U. S. minority population (24).

Most traditional Asian/Pacific diets are rice staple diets, with additional use of other starchy foods such as wheat, rice noodles, tubers) (21, 22, 25, 26, 37). Staple foods are supplemented with seasoned food mixtures which are population-specific. Fish and seafood intakes are higher in traditional Asian/Pacific than in average U. S.diets. Muslims and Hindus from the Indian subcontinent may be vegetarian or have taboos against consumption of beef and/or pork (39); some are vegetarian. As noted previously (Table 4), many Asian/Pacific American foods and seasonings are extremely high in sodium. Examples include bean sauces, dried shrimp, dried salted fish, pickled vegetables, fish sauce, monosodium glutamate, soy sauce, miso, salted eggs (22, 26, 37, 39, 40). Dairy product use is low compared with that of whites. Traditional sources of calcium include tofu, green leafy vegetables and sardines.

American Indians

There are several hundred American Indian tribes in the U. S. (23). Traditional dietary patterns vary according to tribe, geographic region, cultural, and economic traditions (21, 25-27, 41). For example, Indians who live in coastal regions traditionally have high fish and seafood consumption. Indians in mountainous areas traditionally consumed dried meats and fresh water fish. In the Southwest, traditional dietary patterns of Indians are similar to those of Mexican Americans rather than to diets of Indians from other regions. Corn is a staple food in many Indian diets, although manufactured wheat tortillas have replaced handmade corn tortillas. Fried bread dough ("fry bread") is used extensively by many tribes. Indian diets may be characterized by a high carbohydrate,

high sodium, and high saturated fat content and relatively low content of meat and dairy products, with many foods fried and breaded. Consumption of refined sugar products and government commodity foods is characteristic of Indians on reservations. Typical white middle class foods--including bologna, potato chips and carbonated beverages--are used commonly among those with adequate incomes. Certain traditional foods are served only on special occasions.

Current Versus Traditional Dietary Patterns

Minority populations are heterogeneous in numerous respects that influence food intake: for example, sub-ethnic cultural origin, nativity, duration of residence in the U. S., region and community of residence, socioeconomic status and social mobility. Moreover, as the proportion of racial/ethnic minorities in the U. S. population increases, there is an increasing degree of mutual overlap in food choices of different minority and non-minority subpopulations.

The persistence of traditional dietary patterns among U. S. minority populations is not well documented. This type of data is not collected routinely in nutrition surveys. Anecdotal reports of nutritionists in direct contact with minority populations suggest that traditional food preferences continue to influence dietary patterns and are critical variables in dietary counseling (35, 37, 42, 43). Deviations from traditional food patterns probably increase with increasing years of residence in the United States. However, the American foods which are accepted or rejected for reasons of ideology or preference are difficult to predict and may be very specific to interactions between community of origin and community of residence, among other factors (21). Cultural foods may be used more often on weekends than on weekdays (30) but may also be used consistently (37).

Some members of minority groups will adhere closely to traditional foodways, while others will completely adopt typical U. S. meal and food intake patterns, and others will be at various points between these two extremes. Dietary acculturation may differ markedly with age, within and among individuals. Children and adolescents may be the least and elderly persons the most traditional (21, 22, 37, 44-46).

Nutrient Intakes

Different combinations of foods result in similar nutrient intakes, especially for nutrients that are widely distributed in foods. One population group may consume small quantities of very high sodium dense foods (soy sauce or fish paste in Asian/Pacific diets for example), while another may consume large quantities of moderate sodium dense foods (processed breads and breakfast cereals in Black American diets for example), with the same net nutrient intake.

Data on macronutrient intakes of minority groups indicate that a diet composed of 16-20 percent protein, 35-40 percent fat, and about 45-48 percent carbohydrate is characteristic (20, 30, 31, 47-50). Some statistically significant differences in macronutrient intakes have been reported, for example between Mexican Americans and Anglo Americans in San Antonio, Texas (slightly higher carbohydrates intake among the Mexicans) (20). However, these differences are small and may not be biologically important. Moreover, methodological considerations suggest a need for caution in interpreting small differences in nutrient intakes, particularly across studies and over time. The inherent imprecision of dietary assessment, including differences in the nutrient data bases used, may introduce artifactual differences. Data that rely on weekday 24 hour recall interviews may miss important sources of calories consumed primarily on weekends (51). The treatment of alcohol calories also varies across studies, and differences in alcohol use among population subgroups within studies can affect conclusions about dietary patterns (20).

There is evidence of high sodium intakes and low potassium intakes among U. S. blacks (that is, high or low when evaluated by the criteria in Table 2) (52-54). In similar regions and socioeconomic groups, blacks may have sodium intakes that are slightly less than or equivalent to those of whites but lower potassium intakes compared to whites (52). Urinary electrolyte excretion data (52-53) are more convincing evidence of sodium intake than dietary data (54) in this respect, since most dietary studies fail to account for discretionary salt use.

A cross-cultural comparison of 24 hour electrolyte excretion among young adults in Hawaii sug-

gested high sodium intakes (mean 24 hour excretion in the range of 3 to 4 grams of sodium per day) in five Asian/Pacific American ethnic subgroups (55). Sodium/potassium ratios were high also (1.5 to 2.0). In all Asian/Pacific subgroups, sodium excretion was higher than in a Caucasian comparison sample and, in men, potassium intakes in the Asian/Pacific subjects were lower than in whites. However, these may have been chance findings. With large standard deviations in electrolyte excretion, the differences in mean electrolyte excretion levels were not statistically significant.

Not surprisingly, the clearest differences in nutrient intakes between U. S. minorities and whites (non-Hispanic) relate to nutrients in dairy products (e.g., calcium, potassium, vitamin A). Lower consumption of dairy products and a proportionately greater contribution of non-dairy foods to calcium intakes have been documented in several minority populations (15, 21, 26, 34, 39, 56-58).

Obesity

Obesity emerges early in the course of the epidemiologic transition towards the disease patterns of industrialized societies (1), and quickly reaches a high prevalence as caloric intakes increase and physical activity levels decline. When it does appear in previously undernourished societies, obesity may be viewed as a sign of good health and prosperity (1, 22, 59). A striking excess of obesity has been documented in most U. S. minority population subgroups (7, 21, 26, 60-66). For example, in the 55-74 year age range, where hypertension prevalence is 45-54 percent among black men and 62 to 77 percent among black women, approximately 26 percent of black men and 60 percent of black women are overweight (7). Similarly, among 55-74 year old Mexican Americans, 30-37 percent of men and 50-57 percent of women are overweight, and hypertension prevalence ranges from 48 percent to 67 percent among Mexican Americans in this age range (7). Although not systematically documented in national surveys, a high prevalence of obesity in American Indians is reported frequently and across several Indian subethnic groups (21, 66, 67). Pacific Islanders can be included among the U. S. minority groups with a high prevalence of obesity (60, 62,), but obesity is not observed consistently in other Asian American subgroups (21, 68).

Alcohol Intake

Several surveys, including the National Health Examination Survey (69), the National Health Interview Survey (70), and the Behavioral Risk Factor Survey indicate lower than average levels of alcohol intake among black Americans (71). Still, a subset of black Americans who are heavy drinkers can be identified (5). The National Health Interview Survey (70) indicates similar or somewhat lower percentages of alcohol users and heavy drinkers among Hispanics (ethnicity not further defined) compared to whites, but the proportion of heavy drinkers (>5 drinks per day at least 5 times per year) was higher among Hispanics than non-Hispanics in the age group 30-44 years in men and above age 30 years in women. Alcoholism is a widespread problem in the American Indian population (41). However, some Indian tribes have lower than average prevalence of alcohol use (5). Alcohol use is reportedly lower than average among Asian Americans, although not necessarily among Pacific Islanders (5). Asians from the Indian subcontinent may not use alcohol for religious reasons.

Summary and Conclusions

At the cost of having to make potentially misleading generalizations based on a sparse and uneven data base, I have attempted to highlight dietary risk factor issues related to hypertension in U. S. minority groups. Dietary patterns can be described in terms of either nutrient intakes or food consumption. Nutrient intakes relate to biological exposures and, therefore, to the possible need for preventive dietary interventions. Food preferences and food consumption patterns that contribute to these nutrient intakes determine perspectives for dietary change.

The traditional dietary patterns of American Indians and other minority group Americans with origins in Latin or Central American, Africa, the Caribbean, East and Southeast Asia, and the Indian Subcontinent include a wide variety of foods. Some of these foods are familiar to Americans, and some are exotic. For combined cultural and socioeconomic reasons, minority group dietary

patterns include some foods that are problematic for hypertensives or hypertension-prone persons. The most striking problem is high sodium foods. Obesity is another widespread problem among minority groups, and heavy drinking is or may be an additional problem needing attention in some subgroups. The dietary patterns of U. S. minority groups are also characteristically somewhat low in dairy products, and this may limit intakes of potentially protective nutrients such as potassium.

Cross cultural differences in nutrient intakes within countries are much less striking than such differences across countries. Within a shared environment where all intakes are in a physiologically high range, the possibility that dietary patterns are permissive rather than critical for the expression of hypertension should be considered. However, in spite of similarities in overall nutrient intakes or of uncertainties about the role of nutritional factors in hypertension causation, dietary change clearly has a role in hypertension therapy in minority as well as non-minority populations (4).

In conclusion, hypertension offers continuing challenges for students of nutritional epidemiology and behavior. This is especially true where racial/ethnic minority groups are concerned. On the surface, dietary patterns are "modifiable risk factors." However, the dietary factors targeted for change may be associated with culturally unique flavors, with traditional food preservation, with survival, or with prestige. Given the numerous forces in favor of a convergence of dietary patterns among U. S. residents, the cultural food practices that persist are, by definition, those most highly valued. Therefore, they may be the most resistent to change. Additionally, a preference for certain traditional foods may be accompanied by indifference to or dislike for the types of American foods or seasonings that would be lower risk substitutes.

More thinking and rethinking must be done about the feasibility, and perhaps the desirability, of attempting to change certain food practices. Thus, along with research to elucidate the role of nutrition in the etiology and course of hypertension, research to elucidate considerations for changing dietary patterns among all population groups at risk for hypertension is of high priority.

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Table 1
Major Nutrients and Possible Mechanisms for Influencing Blood Pressure

Calories and Macronutrients	Possible Mechanisms
Total calories	Obesity Energy Generation
Carbohydrates (and alcohol)	Energy metabolism Membrane synthesis Insulin regulations--sodium excretion Catecholamine regulation--vascular tone
Proteins	Protein/peptide synthesis Control of cellular function Membrane transport systems
Lipids	Energy source Cell membrane components Prostaglandin synthesis
Electrolytes and Minerals	
Sodium	Intravascular volume Hormone regulation Membrane potential
Potassium	Vascular tone Hormone regulation Cation transport
Calcium	Receptor-ligand binding Hormone synthesis/release Vascular tone Contractile protein interactions
Magnesium	Regulation of calcium channels ATP production Contractile protein interaction
Phosphorous	Membrane structure ATP-energy metabolism cAMP component
Trace elements	Copper-vascular integrity Manganese-energy metabolism Chromium-lipid metabolism Vanadium-sodium/potassium ATPase

Source: Adapted from McCarron, Henry, and Morris, Hypertension 4 (Supp III):III-2-III-13, 1982 in The Surgeon General's Report on Nutrition and Health, 1988 (reference 3).

Table 2

Approximate Criteria for Selected, Postulated Dietary Risk Factors for Hypertension

Risk Factor	Definition[a]
Overweight (excess calories)	Body mass index (BMI)[b] >25-27 kg/m^2
High sodium intake	Average daily sodium (Na) intake >2000-3000 mg/day[c]
Low potassium intake	Average daily potassium (K) intake <3000-4000 mg/day[d]
Low calcium intake	Average daily calcium (Ca) intake <800 mg/day[e]
High alcohol intake	Average daily intake of > 1 oz of ethanol per day[f]

a These definitions refer to healthy persons aged ≥25 years.
b BMI = weight (kg)/height (m)^2; this BMI range reflects the Metropolitan Life Insurance, National Center for Health Statistics, and Bray criteria for defining obesity (9).
c The estimated safe/adequate Na intake for adults is 1100-3300 mg/day (10); sodium intake <2 g/day is associated with blood pressure reduction in hypertensives (4).
d The estimated safe and adequate K intake for adults is 1875-5625 mg/day (10); the midpoint of this range is 3750 mg.
e The adult Recommended Dietary Allowance for calcium (10) is used here as a guideline.
f As recommended by the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (4) and the Surgeon General (3).

Table 3

Mean Daily Intake[a] of Food Energy, Nutrients, and Food Components for Men, Women, and Young Children From the Continuing Survey of Food Intakes by Individuals (CSFII), 1985[b]

	Men	Women	Children
Total Food Energy (% REI)[c]	(94)	(82)	(100)
Fat [% total energy]			
Total fat	[36]	[37]	[34]
Saturated fatty acids	[13]	[13]	[14]
Monounsaturated fatty acids	[14]	[14]	[12]
Polyunsaturated fatty acids	[7]	[7]	[6]
Cholesterol mg	435	304	254
Protein			
[% total energy]	[16]	[16]	[16]
(% RDA)[d]	(175)	(144)	(222)
Carbohydrates [% total energy]	[45]	[46]	[52]
Dietary Fiber g	18	12	10
Minerals			
Calcium (% RDA)[d]	(115)	(78)	(105)
Sodium (ESADDI)[e]	(exceeds)	(within)	(exceeds)
Potassium (ESADDI)[e]	(within)	(within)	(1-3 years exceeds) (4-5 years within)

a Estimated mean daily intake is expressed in several ways: amount of intake, percent of total energy intake, percent of Recommended Dietary Allowance, or comparison with Estimated Safe and Adequate Daily Dietary Intake.

b Data based on 1-day dietary recalls obtained by personal interview for 658 men 19 to 50 years of age, for 1,459 women 19 to 50 years of age, and for 489 of their children 1 to 5 years of age in 1985 (unweighted numbers). Nutrient intakes do not include vitamin and mineral supplements or sodium from salt added at the table.

c Recommended Energy Intake (NRC 1980); Source of percentages: NFCS, CSFII Report Nos. 85-1 and 85-3 (USDA 1985, 1986). (See references 10, 13, 14)

d Recommended Dietary Allowance (NRC 1980); Source of percentages: NFCS, CSFII Report Nos. 85-1 and 85-3 (USDA 1985, 1986). (See references 10, 13, 14)

e Estimated Safe and Adequate Daily Dietary Intake (NRC 1980). (See reference 10)

Source: The Surgeon General's Report on Nutrition and Health, 1988 (reference 3).

Table 4

Sodium Content of Common Filipino Foods

Dried shrimp	3,321 mg per T
Hipon bago-ong[a]	360 mg per t
Patis[b]	340 mg per t
Tinapang tamban[c]	5,689 per 1/2 C
Instant noodles	2,330 per 1/2 C
Tawsi[d]	7,800 per 1/2 C
Chorizo[e]	2,170 per 100 gm

[a] salted and fermented tiny shrimp
[b] concentrated juice of salted fish
[c] smoked Indian sardine
[d] fermented black bean paste
[e] one whole Chinese sausage, cooked

Source: reference 22

First Scientific Session - Discussion

Dr. Ahmed:
I have a question for you Dr Edozien. The nature of the data that you presented to us was ecological. How would you conclude anything from ecological observations?

Dr. Edozien:
The epidemiologic study analysis was used to develop testable hypotheses and I tried at the end to show rather briefly that practically every conclusion from the epidemiologic study was confirmed in feeding experiments in the rat. I also have data on the guinea pig. The epidemiologic study only helped us to develop the hypotheses. But the proofs are in the experimental studies.

Dr. Ahmed:
Do you have levels of statistical significance for the various results?

Dr. Edozien:
All the results, as I have said, are in the presentation. If we begin to put "SEM" in all of them, the tables become very complicated. In all of the slides, I have shown the "SE" for one group which is very similar to all the "SE's". It gives you an indication of the level of significance. But in the results themselves, as you see in the manuscript, only the results that are different at the .05 level have been reported as being different.

Dr. Grim:
Sounds like there are not much data available on dietary habits. Are there plans or designs under way to give us more data? What is the status of this and what will we hear five years from now?

Dr. Kumanyika:
I think one problem we won't be able to overcome and this is the diversity, so that if we get data they will be and I think more of a problem for the smaller groups because blacks are probably more like each other than all the other groups. We won't be able to overcome that in the National Health Surveys.

In Hispanics, HNANES will take care of some general descriptors for three subgroups. The other place where we might actually get
data will be from studies funded by the National Cancer Institute, because they have an aggressive program related to risk reduction and they believe that diet affects cancer risk. So they are funding research, some of which involves diet, which might generate small scale studies of specific groups. They will improvise vitamin A and fiber, but they will also pick up information on micronutrient intakes.

They probably will not tell us much about salt but it's hard to measure.

Anonymous:
Would you also comment on the need for nutrient analysis of ethnic foods? We published something in the Journal of Food Science a few years ago where a particular type of algae preparation that women eat actually has more calcium and greater bioavailability of calcium than cow's milk.

Dr. Kumanyika:
I think that's really important, especially for calcium. Because of time, I did not go into examples on calcium, although they are biologically some of the most interesting because the epidemiology of calcium and calcium-related health problems is backwards to what people would expect. The populations with relatively low rates of osteoporosis, are the ones with low calcium intakes and you would expect it to be the other way around.

I think some of that probably has to do with underestimation of calcium intake because those of us who still chew the chicken bones as well as the

chicken know that you can get calcium that is not going to be in that food table. Also, the preparation methods and so forth that you mentioned will really add calcium or extract calcium in different ways.

I don't know; - In the case of Indian foods, I have seen more literature on analysis of American Indian foods and may be Brenda will talk more about that.

The Surgeon General's Report, if you get a copy, as far as I have found so far, and I have not studied it, does not mention special population issues at all. I flipped through it and I looked at all of the categories where I thought they would mention them, and they treat the dietary risk factors as if they are all one population.

Dr. Edozien:

If I may comment on that, as you could see from some of the slides I showed, calcium is probably the most highly regulated nutrient in the body. The plasma calcium and the retention of calcium in the body have very little relationship to calcium intake. Now people in the Third World countries, even though they have low calcium intake, retain more, and that is why they have less osteoporosis.

The factors involved in the retention of calcium are quite complex. First of all, there is the absorption of calcium, in which parathyroid hormone is involved, and, many nutrients, particularly carbohydrates, influence parathyroid hormone, so a high carbohydrate intake increases parathyroid hormone secretion and improves calcium absorption.

Dietary fat, as we have seen before, reduces ACTH, and ACTH is very strongly involved with calcium retention. Low ACTH results in low calcium retention. Alcohol and carbohydrates increase calcitonin, and calcitonin puts calcium into the bones. The mechanisms for the regulation of plasma calcium are very detailed and complex, and dietary calcium has very little bearing on plasma calcium and the retention of calcium.

Dr. Enwonwu:

There are many reports which suggest that perhaps we are overplaying the role of sodium with respect to hypertension. Some investigators, in fact, incriminate chloride rather than sodium as a factor involved in hypertension. I wonder if any of the speakers this morning would like to comment on the present status of this controversy. Secondly, for Dr. Edozien, on the role of calcium, some reports simply indicate that on a high protein intake with low phosphorous intake, there are dramatic losses of calcium and zinc in urine.

Do you think that could play some role in the regulation of blood pressure?

Dr. Guyton:

In regard to sodium, there are some populations in the world that have sodium intakes less than 1/100th of other populations,
so why don't all these populations that have a high sodium intake have just astronomical blood pressures in relation to those who have very low sodium? Now the difference in blood pressures, you take those of the northern Japanese, blood pressure on the average would, let's say the mean pressure, instead of the normal of 100, might be as high as 120 or something in that order. You take the Indians in the upper Amazon valley where the sodium intake is 1/100th that in the northern Japanese area, the mean blood pressure might be something in the order of, say 85. So there is a difference in pressure of about 35 mm. of mercury, but a difference in salt intake of 100-fold.

Now that shows you, I think, how important some of our internal regulatory mechanisms are, to allow you this tremendous diversity of salt intake. I was talking about the study in Indiana and also a study that we did in animals. We changed the salt intake 50-fold in dogs and got a 4 mm. mercury pressure change. In Indiana they changed it 150-fold and got a 17 mm. pressure change.

However, acutely, we have these powerful feedback control systems like the renin angiotensin system, which will allow us this tremendous change in salt intake, but when your kidneys begin to get into bad shape or when your secretory mechanism or your aldosterone mechanism doesn't work, as in old age, all of these things begin to get impaired, then you become more salt susceptible.

Now we can show this in actual experiments because we can make an animal have a poor renin

angiotensin system. In that case, the animals are always very salt sensitive. The amount of salt, from a low salt to a high salt, can change blood pressure 40 and 50 mm. of mercury. So, with the angiotensin system not working, the animals are always very, very salt sensitive. Now the next question is, if you take a high salt diet over a period of a lifetime what does that do? Does it change any of these internal mechanisms? We know most of the experiments that have been done have been acute experiments.

The experiments I quoted a moment ago, where we increased the salt intake in dogs 50-fold, were acute experiments over a period of a month and they had only 4 mm. mercury change in pressure. Now what about over a lifetime? There are many other studies which are nutritional type studies. They are not really physiological studies. But true enough if you give an excess of salt, particularly to animals who are already hypertension sensitive, like the spontaneously hypertensive rat, and like the dull hypertensive rat, give them excess salt, then they are also much more salt sensitive over a period of months than are the normal rats.

So there seems to be a generic susceptibility in some animals, and I expect in human beings, whereby, over a long period of time, they are very salt sensitive. In some instances, you give them all of this salt over a period of time they get the hypertension, you take away the salt and hypertension does not go away, indicating that there is much more than just the basic physiological mechanisms involved and that over a long period of time the salt seems to cause actual permanent structural changes, and I would guess mainly in the kidney tissue. That causes the hypertension to persist. So I think salt is a very important feature. It is certainly a keystone to natural normal blood pressure control.

We have beautiful control systems that allow us to take in tremendous amounts of salt but if these go wrong, and I think that in certain genetic populations they are wrong, than over a lifetime of salt intake you are going to get both the physiological and the structural changes which will follow from this high salt intake. So, I don't think that issue has gone away by any means. I think we are just understanding it more.

Anonymous:

I know Dr. Thomas is going to be here this afternoon, but I guess he's not making a presentation about the cohort study. But one question that some people have raised about the cohort study is that we are dealing with a population of people who are now of a high socioeconomic status, and therefore their diets have changed, but they in fact grew up in poverty and so one of the questions is, if people grow up eating high sodium diets, but later on in their lives their diets change to low sodium, high potassium, what impact does that have? Do they continue to have a high prevalence of hypertension? Of course, in the cohort studies, the Meharry graduates continue to have a very high prevalence of hypertension compared to John Hopkins cohorts. Can you comment on this? Are you familiar with this?

Dr. Thomas:

I do not think the data on the Meharry cohort have changed much. But I think they are probably getting similar diets as to when they were premed students, probably getting more; they get more stakes and other highly seasoned foods. But we have not been able to detect any definite, qualitative change in their diet. It seems to me that the pattern for development of hypertension is established in the formative years. Before they even come to medical school, I think they have set the stage for greater hypertension in adult life. I do not think that once they graduate
that this pattern changes.

Actually, our data show that a greater percentage of our students came not from low socioeconomic homes. Probably 40% of them were from parents who were school teachers and skilled labors, like that, so we did not group them in the low socioeconomic status. It seems to me that the stage was set during their formative years in terms of habits and we have not seen any changes in that.

Dr. Grim:

But it is true that it is felt that the low socioeconomic diet, the poverty diet, is generally higher in sodium and lower in potassium.

Dr. Thomas:

Yes

Dr. Grim
I am a little surprised at that data. Are you saying that at least 40% of them were not low socioeconomic?

Dr. Thomas:
Right.

Dr. Grim:
Thank you.

Dr. Edozien:
First of all, I have one or two words to add, if I may be permitted to do so, to what Dr. Guyton has already said with regard to sodium. I believe that two statements which seem to be contradictory are both true. The first is that sodium does have a tremendous impact on blood pressure and on the development of hypertension. And the second is that dietary sodium has little or no effects on blood pressure. I think both statements are true.

Now with regard to dietary sodium, the regulatory mechanisms are very strong, so that when you have a high intake of sodium, you set into machinery the mechanism to excrete the sodium, and if you have low intake, you set the machinery in motion to retain sodium. And so dietary sodium triggers regulatory processes and has very little effect on blood pressure. But anything that will lead to sodium retention over and above the normal will increase blood pressure and sodium intake alone does not seem to be able to do this.

Other factors, like renal disease, which I forgot to mention, in which you retain sodium, will produce an increase in blood pressure. Norepinephrine and calcium - they retain sodium and they increase blood pressure. Calcium by reducing serotonin, reduces the production of hemoglobin and the red cell mass. And so two things are involved with calcium, the retention of sodium and the decrease in blood volume, due mainly to a fall in the red cell mass. For that reason calcium by itself does not seem to have too much effect on blood pressure, but norepinephrine, ACTH, cortisol, things that retain sodium and do not alter the hemoglobin production, have a tremendous impact on blood pressure.

With regard to the question which Professor Enwonwu asked on the role of protein and phosphorous, both protein and phosphorous alter glucagon and therefore alter calcium retention. The mechanisms of their involvement in blood pressure regulation is through calcium. Quite interestingly, protein experimentally has a different role in man than in rats. In both species protein, because of the effect of tryptophan and niacin, reduces glucagon. But in man, low glucagon leads to calcium retention because in man glucagon excretes calcium, but in the rat glucagon retains calcium and so protein has different effects on glucagon, on calcium, and on blood pressure in man and in the rat.

Dr. Rogel
Yes, I have a question for Dr. Edozien. My question is about Vitamin C. You several times mentioned that because the American Hispanics have a low intake of this vitamin, there are many changes that are going on in their hormones, and so on, and also in their distribution of body fat. I wonder if you could comment more on that - on how you derived those conclusions, whether you did some animal studies or whether you had some regression analysis. And then, would you comment on how vitamin C may be involved in hypertension, if you believe there is any connection.

Dr Edozien:
Well I thought I dealt with that matter, but there are so much data that it might have been skipped. Now, this group of Mexican Americans were migrant workers, and the main thing about their diet was very little consumption of fruits and vegetables, that is they had a low vitamin C. We couldn't for a long time determine the cause of the hormonal changes in that group until we were able to identify the relationship between IgG and norepinephrine.

Once that was done then we began to see that there were some areas in which the Mexican Americans resembled blacks and some areas in which they were in opposite directions, and that's gradually how we came to the conclusion that those areas where they were different might be due to norepinephrine, and this could be validated in the guinea pig. The particular role of vitamin C is that vitamin C, by increasing norepinephrine, reduces dopamine hydroxylase, and we see those things where norepinephrine is in-

volved, like retention of calcium, retention of sodium, blood pressure, the synthesis of serotonin, the synthesis of ovarian hormones - vitamin C is involved with these.

But in the metabolism of body fat, particularly in the biceps area, blacks and Mexican American are very similar in terms of muscle mass, so these we hypothesize were due to DOPA.

I responded to the question earlier, but this epidemiologic study helped us, through regression analysis, to make associations, and once we had made the associations it was very easy to know what to look for. So we could work experimentally in animals knowing what to look for.

Once we knew what to look for, the animal experiments were easy. Everything we have concluded from the epidemiologic study, we could prove experimentally.

Dr. Rogel:

Well then, would you suggest that blacks eat less vitamin C?

Dr. Edozien:

The cure may be worse than the disease. Afterwards, they have a high level of norepinephrine for a specific reason and the hypothesis why we think they have this high level of norepinephrine may be that they need more dopa for the synthesis of the melanine pigment and since dopa is starting substrate for both norepinephrine and melanin. The increase in norepinephrine might be incidental to the increased production of dopa.

The second possibility, which I think is more likely, is that blacks, because of the pigment itself, absorb less ultraviolet radiation, so they produce less vitamin D and they have low absorption of calcium, which can be proven. If they have low absorption of calcium, then in order to survive they need to retain more calcium. This may be the reason for the development of this high level of norepinephrine in the evolutionary process. So there is a reason for it to be there. To disturb it or try to prevent it from occuring might do more harm than good.

Dr. Enwonwu:

This is an area of special interest to our Center for Nutrition so I take the privilege of asking the last question for the morning. The question relates to the role of histamine in hypertension. There are now several articles showing that many women at various stages of pregnancy tend to lose vitamin C from the tissues, and there is an inverse relationship between vitamin C status and the metabolism of histamine. As blood vitamin C level drops, blood histamine content increases. Do you see any role for histamine in pregnancy associated increase in blood pressure?

Dr. Edozien:

Histamine is central to the roles of norepinephrine and calcium in the regulation of blood pressure. You can show this quite readily in the rats. Both calcium and norepinephrine will reduce plasma histidine and increase the production of histamine. I think that it is the histamine that effects the conversion from angiotensin I to angiotensin II.

So the whole area of blood pressure regulation as well as sodium retention associated with calcium and norepinephrine is probably mediated through histamine.

Second Scientific Session

Chair **John Thomas, M.D.**

THE WORLDWIDE EPIDEMIOLOGY OF HYPERTENSION IN BLACKS WITH A NOTE ON A NEW THEORY FOR THE GREATER PREVALENCE OF HYPERTENSION IN WESTERN HEMISPHERE BLACKS.

Clarence E. Grim* and Thomas W. Wilson
Hypertension Research Center
Charles R. Drew University of Medicine and Science
and the King/Drew Medical Center
Los Angeles, CA 90059

In the Western Hemisphere, hypertension or high blood pressure is the major health problem of the black community. It is the number one health problem because it is so common and because the long term effects of high blood pressure are so devastating on the health of those afflicted. A recent survey of a random sample of the population of the state of California determined that in census tracts that were predominantly black, a staggering 44% of black males between the ages of 45 and 64 had uncontrolled hypertension and another 27% had controlled blood pressure. Thus 71% of black males 45-64 years in the inner city suffer from hypertension, the major contributor to heart disease in blacks (1). These rates are twice the rates seen in non-black populations. As reported elsewhere in this volume by Nesser and Thomas, hypertension in blacks is not limited to those of lower socio-economic class as over 40% of Meharry Medical School's black male students have developed hypertension within 20 years after they have graduated from school. Other reports in this volume detail the epidemiology and complications in US blacks. The current paper will review the history of the epidemiology of hypertension elsewhere in the world and suggest a new hypothesis relevant to the greater prevalence of hypertension in western hemisphere blacks.

High blood pressure is the major chronic health problem in all industrialized societies. High blood pressure kills because it eithermakes blood vessels rupture, decreases blood flow to critical tissues, accelerates the process of atherosclerosis leading to blockage of blood vessels or the heart fails because it can no longer generate the force necessary to circulate the blood. There is now conclusive evidence that pharmacologic treatment of hypertension can markedly reduce the risk of death from these causes.

Hypertension in the black Community

Hypertension or high blood pressure is the major health problem of the Western black population because it is so common and because it affects blacks from the moment of conception to old age.

The devastating effects of hypertension begin in the unborn black. The high prevalence of hypertension in black women makes it more likely that pregnancy will occur in someone who already has hypertension. If a mother doesn't have hypertension when she gets pregnant, she is more likely to develop it during pregnancy. Hypertension decreases blood flow to the fetus which stunts its growth. Small birth weight is the major contributor to perinatal death and illness in black babies. Western hemisphere blacks have one of the highest rates of premature birth and perinatal mortality in the world. The leading cause of maternal death during pregnancy is hypertension.

During childhood, blacks tend to have higher blood pressure than whites. The Bogalusa heart study, a long term study of the development of heart disease, has reported that fatty streaks (a precursor of overt atherosclerosis or hardening of the arteries) were present in 37% of the aortas of black children and young adults, but were present in

*Speaker

only 17% of the white children. Those children who had a higher blood pressure and a higher blood cholesterol were more likely to have the more advanced evidence of atherosclerosis.

During adolescence, blacks tend to have higher blood pressures than whites and this difference accelerates after age 18. From age 15 to 75 years, blacks die from hypertensive complications at 5 to 10 times the rate for whites. It is well known that the major cause of death (50% of all deaths) in blacks is heart disease. In Los Angeles County blacks are experiencing death due to cardiovascular disease at a greater rate than whites or Hispanics. For example, in blacks less than 35 years of age, deaths due to heart disease are twice that found in whites and 8 times that in other ethnic minorities. In black females less then 45 years of age, death due to hypertension is 11 times that seen in white females. Unfortunately, 40% of these deaths occur suddenly, outside of the hospital. The health care providers for the black population must remember that sudden death cannot be treated. It can only be prevented. Strategies to prevent these unnecessary deaths in the black community must be urgently investigated.

The major cause of kidney disease in blacks is uncontrolled hypertension and blacks are much more likely to need kidney dialysis or transplantation than whites. In southern California one black person has to be placed on the kidney machine every working day because of kidney failure from hypertension. Each new person added to the kidney treatment program increases the cost to Medicare $30,000 for the rest of the individual's life.

In the aging population (65 to 84 years), blacks experience 30% moredeaths due to stroke than do whites, and this is almost certainly related to the greater prevalence of hypertension in elderly blacks. Treatment of hypertension in this age group will decrease strokes by 50%. In summary the major health problem of the black community is hypertension and that community must rise to the banner of HYPERTENSION OR HEALTH.

Why Do People's Blood Pressures Differ From One Another?

As with other quantitative traits such as height and weight, blood pressure differs between people. People can differ from each other in physical traits because they differ in what they have inherited (genotype) that influence the expression of that trait. Thus the final summation of the environment and the genotype results in the phenotype. For example, tall people generally have tall relatives. However if a person from a tall family does not eat well, he may not grow to be as tall as other family members. In a similar fashion, it has been known for many years that people who have high blood pressure are more likely to have someone else in the family with high blood pressure. Traits that occur in families can occur because the family shares common genes (or inheritance) or because the family members share similar environmental factors such as how or what they eat or how they exercise. In white subjects the major source of differences in blood pressure between people seems to be due to genetic (inherited) factors. There are a number of nongenetic factors that contribute to blood pressure variation. Blood pressure increases with age, obesity, alcohol or sodium intake or (possibly) deficiency of calcium or potassium. There are several reasons that we should be interested in finding out if blood pressure is genetic, as well as the role of environment on the variation in blood pressure. Genetic factors are of interest because if we can find a marker for the genetic factor(s) that leads to high blood pressure then we can identify early those at risk and test strategies to prevent the development of hypertension in the future. In addition, if we know the specific cause of hypertension in an individual patient the cause can be treated. Understanding the environmental influences on blood pressure will likely lead us to better ways to prevent or treat hypertension without the use of drugs. This information can be obtained by family studies of blood pressure in parents and their children, from adoption studies and from studies in twins.

When blood pressure is measured in black or white families it has been found that children's blood pressure is more like the blood pressure of their parents or their brothers and sisters than of unrelated adults or children. Similarities in blood pressure in families could be due to:

1.) a common environment shared by the family members such as eating habits, exercise habits,

or family stress.

2.) common (inherited) genes that control blood pressure. Genes can influence blood pressure by a number of mechanisms. These include genetic control of enzymes or hormones that regulate nerves, blood vessels or how the kidney handles sodium and other dietary components that may affect blood pressure.

One method to separate the role of genes from that of environment is to study adopted children. One then finds out if the blood pressure becomes similar to that of the adoptive family. Studies in Canada have found that even when adopted at birth, the blood pressures of white adopted children do not correlate with those of their adopted parents or the blood pressures of natural children of the adoptive parents. This is very strong evidence that blood pressure is set by what children inherit rather than the family environment in which they are raised. There have been no adoption studies of blood pressure in black families.

Geographical Differences In Blood Pressure In Blacks

Since the report by Donnison in 1929 (2), it has been known that blood pressure in Africans was strikingly lower than in Western Hemisphere whites. Three years later, a report (3) of blood pressure in black and white Americans showed that blood pressure was higher in blacks than whites. There has never been a report in the Western Hemisphere in which blood pressure was lower in blacks than in whites. In contrast, a study by Seedat reported that in general blood pressure was lower in blacks in South Africa than in whites. A number of subsequent studies since then have demonstrated that, on the average, Blacks in the Western hemisphere have higher blood pressures than Blacks from Sub-Sahara Africa. Because of the similar genetic heritage of these groups it has been suggested that these differences in blood pressure distribution are most likely due to environmental differences between the two areas. However, a review of the history of the slave trade suggests that the operation of natural selection during this period may have also contributed to these geographical differences in blood pressure distribution we observe today. A similar concept was considered by Blackburn and Prineas (4) but rejected by them as too speculative. Our reading of this period of history lead us to believe they were premature in their rejection (5, 6, 7).

The slave trade was characterized by conditions promoting excessive salt (sodium) loss. We suggest that individuals with an enhanced ability to conserve sodium (Na+) would have had a significant survival advantage over others. This trait, advantageous then, may be medically deleterious in today's world of high Na+ consumption, because it may lead to hypertension (8).

We have compiled the data from over 60 reports (9-69) concerning blood pressure in blacks around the world. This data is summarized in Figure 1. In this figure, we have plotted the blood pressures in various areas around the world from reports in which 40-60 year old men were studied. Because not all of these studies reported a value for the mean, standard deviation and the number of subjects studied, it is not possible to statistically compare these results. There are additional problems in that all samples were not random and the techniques of blood pressure measurement were not standardized. This was especially true for diastolic blood pressure. As can be seen, the lowest reported blood pressures are from Eastern Africa. The greatest variation in blood pressure over (40 mm Hg) has been from studies in South Africa. Blood pressure in West and Central Africa are similar, but also show a variation of over 20 mm Hg. In the United States the highest blood pressures are reported from the older studies from the south east coastal area before there were ways to treat hypertension. Thus the lower blood pressure in US Blacks seen in CHECK(68) and HANES(69) may be related to the fact that many blacks were being treated. Finally, the average blood pressure is highest in the West Indies. Most investigators who have speculated on these geographical differences in blood pressure in blacks have suggested that environmental factors are most likely responsible. Current working hypotheses in this regard point to either behavioral or nutritional factors (70, 71, 72). We suggest that inherited differences in Na+ metabolism as a consequence of selective pressure during slavery accounts for a significant portion of the observed geographical differences in blood pressure among Black popu-

lations.

A genetic contribution to variability in blood pressure distribution in Blacks and Whites has been suggested by familial and twin studies (73, 74, 75). Family and twin studies in white subjects have also demonstrated that the ability to excrete a Na+ load and variations in blood pressure with changes in Na+ intake and with the response to stress are influenced by genetic factors (76, 77). Recent studies have focused on the concept of "salt sensitivity", defined as a significant rise in blood pressure following a "Na+ load" or a significant fall in blood pressure following Na+ depletion (78, 79). Individuals with salt sensitive blood pressure are more common in American Blacks than among Whites (80) and hypertensive Blacks are twice as likely to normalize their blood pressure with Na+ excreting diuretics (81). Afro-Americans have also been shown to excrete a "Na+ load" more slowly than a White control group, which suggests a greater ability of Blacks to retain Na+(82). Biochemical differences in Na+ regulating systems have been reported between American Blacks and Whites. These include lower plasma renin activity (83), but could be due to inherited influences on systems regulating Na+ metabolism. There are precedents for genetic influences on Na+ metabolism in man and animals. Cystic fibrosis is an autosomal dominant trait common in whites but extremely rare in black subjects. These patients frequently die due to excessive Na+ losses in sweat (87). A number of inherited problems lead to hypertension due to increased sodium retention. These include Liddle's Syndrome (88) (a condition of increased tubular reabsorption of sodium reversed by triampterene) and glucocorticoid responsive hyperaldosteronism (89). Several adrenal biosynthetic disorders lead to mineralocorticoid excess and hypertension due to excessive Na+ retention (90). In addition, Dahl and fellow workers were able to selectively breed rats who were sensitive or resistant to the blood pressure raising effects of Na+ (91).

Sodium Homeostasis

Sodium enters the body through the oral route and exits in urine, stools, and sweat. As discussed by Guyton elsewhere in this volume, the regulation of total body Na+ is exquisitely complex and operates around a "set point"(92, 93). Whenever total body Na+ rises above this set point, Na+ is excreted by the kidneys. Guyton and colleagues have elegantly demonstrated the overriding dominance of the pressure natriuresis curve of the kidney on the relationship between total body sodium and blood pressure. When total body Na+ decreases below the set point the kidney avidly retains Na+. The exact nature of the sensors that detect a change in total body Na+ are not clear. Nevertheless, careful metabolic studies on white subjects on a normal Na+ intake (150 mmol Na+) in the United States can usually account for 95% of ingested Na+ by collecting and analyzing sweat, stool, and urine. Of this amount, the kidney excretes 96% of the Na+ while about 2% is lost in the stool and 2% in the sweat (94). Thus, on a daily intake of 150 mmol of dietary Na+, 142 mmol (95%) could be accounted for by 136 mmol of Na+ in the urine, 3 mmol in sweat and 3 mmol in the stool. The acute oral ingestion of sodium chloride leads to rapid activation of natriuretic systems (95) which are able to bring the Na+ balance back to steady state in 8-12 hours. The systems appear to be independent of the renal nerves and adrenal secretions. It seems likely that atrial natriuretic peptide (discussed elsewhere in this volume) may be involved in this response. From a survival point of view, the ability to shed excess ingested sodium would be critical if any animal or man accidentally ingests salty water. On the other hand the ability to retain sodium during times of low sodium intake is a function of the renin-aldosterone system. Intravenous Na+ loading has also been used to study the time course of Na+ excretion after Na+ loading. Using this technique the team of Grim, Luft and Weinberger have demonstrated that the amount of Na+ retained is decreased in first degree relatives of hypertensives (96), and that the rate of Na+ excreted is influenced by age, the level of activity of the renin system, by genetic and by ethnic factors(97).

When non-renal losses of Na+ increase, regulating systems are activated (especially the renin-angiotensin-aldosterone system) which enable the kidneys to attempt to maintain Na+ homeostasis by decreasing Na+ loss in the urine. Once urine Na+ is reduced to zero, non-renal losses as-

sume critical physiologic and survival importance. Indeed, non-renal losses of Na+ can be fatal even when urinary Na+ losses are nil. Conditions leading to fatal Na+ depletion include sweating induced by high ambient temperature, profuse diarrhea or prolonged vomiting associated with sea sickness (98). Table 1 summarizes the values for sodium in the diet, sweat, stool and vomit.

Table 1

Source	Sodium Concentration
Diet	0-600 mmole/24 hours
Sweat	
Not heat adapted	40-80 mmole/liter
Heat adapted	2-80 mmole/liter
Stool	
Normal	2.5-5 mmole/24 hr
Diarrhea	90-133 mmol/l
Vomit	40-60 mmol/l

The Na+ content of sweat in non-heat adapted individuals varies from 40-80 mmol Na+/liter and sweating rates of over a liter per hour can occur. Thus profuse sweating can lead to rapid Na+ and water depletion which stimulates renin release(99). As discussed elsewhere in this volume by Dr. Saunders, renin generates angiotensin I which is converted to angiotensin II. Angiotensin II has an acute anti-natriuretic effect and also stimulates aldosterone, the major Na+ retaining steroid which acts on the renal tubule and the sweat gland. The effect on the latter is to stimulate Na+ reabsorption by the sweat gland epithelial cells and sweat gland Na+ concentration falls to as low as 1.7 mmole Na+/L (100). This process is called heat acclimatization or adaptation. Changes in sweat production rates and electrolyte content are a consequence of heat adaptation. Sweat output is a function of ambient temperature, heat production by the body and work performed. Body heat is dissipated by sweat evaporation, convection, conduction, and radiation (102). At room temperature, for example, only 22% of the heat produced at basal metabolism would be dissipated by sweat. Under these conditions 0.026 l/hr of sweat would be lost, containing 0.04 mmol Na+ in the acclimatized person and about 2.0 mmols Na+ in the unacclimatized person. Thus, under basal conditions, during a 24 hour period, an acclimatized person would lose less than 1.0 mmol of Na+ through sweating, but an unacclimatized individual could lose as much as 50 mmol Na+.

Sodium excreted through the sweat, however, increases dramatically as the ambient temperature rises. This is mostly related to the fact that under high sweating rates the progress of fluid through the sweat gland is so rapid that there is little time for the Na+ to be reabsorbed by the epithelia cells. Under extremely high ambient temperatures, up to 640 kcal/hr of heat may need to be removed from the body (35). If all of this heat were dissipated by sweat, water loss during each hour would be about 1.1 liter and Na+ loss would vary by acclimatization. The most highly acclimatized individual would lose about 2 mmol Na+/hr, but the least acclimatized would excrete almost 90 mmol Na+/hr. Regardless of the degree of acclimatization, lengthy episodes of this heat dissipation by sweating could be dangerous if Na+ losses were not replenished. Obviously, an individual with high body Na+ stores would have a greater degree of protection against fatal Na+ loss through excessive sweating. In other words, individuals who are good at storing salt in the body would be less likely to die of sodium depletion.

Fecal excretion of Na+ under basal conditions is very low (2.5 mmol-5.0 mmol/day), but rises rapidly with diarrhea(103). Cholera produces the most severe Na+ losses averaging 133.0 mmol Na+/L in stools and fatal Na+ depletion can occur within a few hours. Even non-cholera diarrheal stools contain about 97 mmol Na+/L(104). Finally, vomit can contain up to 60 mmol Na+/L, and can be another dramatic source of Na+ loss(105). Clearly, Na+ loss through sweat, diarrhea, and vomit can lead to fatal Na+ deficiency unless there is adequate ingestion of Na+ to replace these losses.

Evolution of Salt Conservation

Because of the key role of Na+ in maintaining the internal milieu, an enhanced ability to conserve Na+ under conditions of low intake or losses from sweating, diarrhea, or vomiting would have a tremendous survival advantage. In 1967 Helmer suggested that in sub-Saharan Africa, evolutionary adaptations to low-salt hot environments would emerge to protect against fatal volume depletion from excessive sweating. Thus, salt-conserving individuals would have a selective advantage. In an environment rich in dietary salt, and in the absence of excessive sweating, Helmer believed that this enhanced salt-conserving ability would lead to Na+ retention and hypertension (106). We suggest that diarrhea and vomiting losses should be added to Helmer's thesis of the evolution of "salt conservation" and restated as follows:

An enhanced genetic-based ability to conserve salt would tend to increase in frequency in populations experiencing fatal Na+ losses in sweat, or stools, or vomit.

We will now examine evidence for this modified hypothesis from records of the trans-Atlantic slave trade. In the following discussion, we will use the term "Na+ conserver" for individuals who are better than others at retaining Na+ under high or low Na+ intakes.

Trans-Atlantic Slave Trade

Although slavery existed since recorded history within Africa, the expansive trans-Atlantic slave trade of Africans began in the early 16th century (107). The primary purpose of the Atlantic trade was to supply cheap human labor to the plantation economy of the New World. It ended by the late 19th century but during the nearly 400 years of the trade more than 12 million Africans (mostly from West and Central Africa) were transported to the Western hemisphere (108). Most of the transported captives were healthy young men (109). Sweating and gastrointestinal disorders were very common during the slave trade.

After being seized in the interior of Africa, the captives were transported, either on foot or down rivers, to the sea. There they were confined in small shelters (barracoons) along the coast to await transport. After individual captives were loaded, the slave ship often cruised along the coast for more than three months until it had a full load. The ship then began its voyage across the Atlantic ("middle passage"), often traveling for several months before the captives were unloaded in the Caribbean islands or on the mainland of America (110). During these various stages of the slave trade many of the captive Africans died. A review of the causes of death and the conditions of the slave trade suggests Na+ depletion played a major role in these deaths. We will first examine the record for Na+ depleting conditions and then review what is known about salt intake.

Table 2 divides the first two years of a captive's life into several critical points for survival as reported by various historians(111-115).

Table 2

THE ESTIMATED MORTALITY DURING THE FIRST TWO YEARS OF THE LIFE OF A CAPTIVE SLAVE

Critical points for death	Percent Mortality (per cent)	Cumulative Survival (per cent)
1. Capture	10?	90
2. March	10?	81
3. Factories	5?	77
4. "Slaving" the Coast	12	73
5. Middle Passage	12	64
6. Quarantine	5	57
7. Transport to worksite	5?	54
8. "Seasoning"	20	43

The true mortality was probably higher as investigators suspect that there was underreporting of deaths(116). The data in the mortality column are the estimates at each step in the slave trade. The question marks in the table are due to the fact that there are few good records to document mortality at these points. The cumulative survival column

was obtained by multiplying the proportion surviving at each point by the proportion surviving at the previous point. For example, if we start with 100 potential captives and 10% died during capture, the survival would be 90%. The proportion surviving would be 0.9 (90/100). On the march to the coast the proportion surviving was again 0.9 (10% mortality). The cumulative survival is given by the product of 0.9 times 0.9 or 0.81. Thus 0.81 or 81% of the original population survived the march to the sea.

CAPTURE: Estimates of the mortality during capture vary from 5 to 90%. It is not likely that survival at this point was related to the ability to conserve sodium.

MARCH TO THE COAST: Mortality during the march to the coast has also been difficult to determine as data are lacking, but current estimates are about 10%. Salt and water deficiencies were likely during this march. The French traveler, Caillie, noted the apparent effects of excessive sweating among the captives. He wrote in the early 1800's that:

"...nobody suffered more intensely from thirst than the poor little slaves, who were crying for water. Exhausted by their sufferings and their lamentations, these unhappy creatures fell on the ground, and seemed to have no power to rise." (117).

HOLDING IN BARRACOONS: It could not have been too different on the coast. Those who made it were confined in small buildings known as barracoons. Body heat produced in these crowded structures would cause more sweating and salt losses. We estimate mortality at a conservative 5%.

"SLAVING" THE COAST: Individuals able to survive the march to the coast and the barracoons were then loaded onto the ships where they may have remained for months while the captain sailed up and down the coast of west Africa to get a full (and therefore profitable) load of captives. This process was termed "slaving" the coast.

THE MIDDLE PASSAGE: The best documented portion of the trade was the infamous middle passage (118). Historians have estimated the average daily death rate on this voyage was 2 per 1000 captives per day. This resulted in at least a 12% mortality from the time of leaving the African coast to arrival in the Western Hemisphere. During the first days on the ocean more than a quarter of unaccustomed passengers suffered from sea sickness (119). Alexander Falconbridge, a surgeon on several slave ships, noted this when he stated that the captives "are far more violently affected by seasickness than the Europeans."(120) This acute vomiting could result in severe Na+ losses.

During passage, the Africans usually remained below deck, although at times small groups were allowed on deck for exercise and fresh air. Below deck, the port holes were usually open for ventilation, but the insufficiency of this was apparent from the words of one African survivor of the middle passage:

"The closeness of the place and the heat of the climate, added to the number in the ship, which was so crowded that each had scarcely room to turn himself, almost suffocating us. This produced copious perspirations, so that the air soon became unfit for respiration from a variety of loathesome smells, and brought on a sickness among the slaves, of which many died(121)."

During storms all port holes were shut tight. Body heat in this confined, unventilated area must have raised the ambient temperature above 100 F. Passengers on the slave ships were so struck with the "horror" below decks that they wrote about the conditions in some detail(122). Again from Falconbridge:

"...But whenever the sea is rough, and the rain heavy, it becomes necessary to shut these and every other conveyance by which air is admitted. The fresh air being thus excluded, the negroes rooms very soon grow intolerably hot. The confined air, rendered noxious by the effluvia exhaled from their bodies, and by being repeatedly breathed, soon produces fevers and fluxes, which generally carry off great numbers of them."(123)(p.24)

Under these hot and humid conditions a better ability to conserve salt would lead to a survival advantage. The disease environment on the ships probably played a selective role as well.

Economic and quantitative historians who have examined records on the "middle passage" have confirmed that the greatest mortality was from "fluxes" and "fevers"(124). "Flux," a term for diarrhea, was the primary cause of death and was a daily killer on many ships. As late as 1824 during

the clandestine voyage of the French slave ship, le Jeune Louis, diarrhea (dissenterie) was responsible for one to five deaths each day during the passage across the Atlantic (125).

Fevers were the second most common cause of death on the ships (126). Attempting to cool the body, the thermoregulatory system produces sweat with it's attendant Na+ loss. A leading expert on the physiology of salt, Derek Denton, observed that with infectious diseases involving electrolyte loss, the initial defence for survival must be the regulation of salt and water balance because one needs to withstand the volume depleting impact of the disease for a few days until immunological mechanisms become effective (127). Again, an enhanced ability to conserve Na+ could mean the difference between life and death.

Fatal heat stroke may have been confused with infectious febrile illnesses as fever and diarrhea are also symptoms of the condition (35). The observation made by the captains and sea surgeons of slave ships of an increased mortality from fevers and fluxes during heating episodes caused by the closure of air passages, suggests to us that many deaths were related in some fashion to heat stroke. However, the Reverend Stephen Hales, a leading physician investigator of the mid-18th century, believed that "noxious putrid Air" accumulated below deck and produced the high death rate. Indeed health problems in confined areas like ship holds (and mines) led him to develop a human-powered "Ventilator" which could be mounted on slave ships (and in other confined areas) to rid these areas of "evil humors". Slave ship captains that used the Ventilator testified to Hale that death rate on slave ships dropped dramatically (128). We suggest his device was effective because it lowered the ambient temperature and humidity in the shipholds. This would decrease sweat-induced Na+ depletion and protect against heat stroke or fatal Na+ depletion from diarrhea, vomiting or low Na+ intake. Unfortunately it appears his device was only rarely employed during the slave trade.

In summary, the conditions of the slave ship journey were conducive to large Na+ losses. To dramatize the extraordinary non-renal Na+ losses, imagine a worst case scenario: a non-heat adapted captive confined for one hour in a hot and humid ship hold, with diarrhea and sea sickness. Losses of Na+ could be 90 mmol in one liter of sweat, 100 mmol in one liter of diarrhea and 60 mmol in one liter of vomit. This one hour loss would exceed 250 mmol of Na+ or about 15 grams of sodium chloride (NaCl). Continuation of such dramatic Na+ losses, not to mention the water losses, would soon be fatal. An extraordinary reservoir of exchangeable Na+ or a tremendous intake of Na+ would be necessary to survive these threats to Na+ homeostasis. Of course, Na+ loss on the slave ship would vary depending on such factors as the environment on the ship as well one's individual ability to lower Na+ loss in sweat, stools, or vomit.

QUARANTINE: Additional mortality occurred after arriving in the West while being quarantined before sale.

TRANSPORTATION TO THE FINAL WORKSITE: The journey to the worksite was frequently on smaller ships and documentation of mortality was poor. Transportation in the final worksite (it is 1500 miles from Barbados, a major receiving port, to the coast of South Carolina).

SEASONING: Mortality during this period was related to exposure to new diseases causing diarrhea, fever, sweating, dietary deficiencies, and from the sever labor required of most slaves. Additional causes of mortality included injury, murder and suicide. This latter process had a mortality of at least 10% per year. One observer stated it was rare to see a slave who had survived more than ten years. In any case, this high death rate or "selection pressure" took place in a time span of less than two years and involved the breeding portion of the African population that had been transported to the West. If the mortality was not randomly distributed among the captives, the survivors must have been different from those who died. Genetic differences would be passed on to the progeny of the survivors. We suggest that the ability to conserve Na+ played a major role in survival under this selection pressure. We will now examine the data regarding salt intake among captives on the slave ships.

Salt Intake

Abundant dietary Na+ might, of course, provides a survival advantage under conditions of

severe Na+ depletion. Unfortunately, because of contradictory evidence, it is impossible for us to estimate accurately the average salt intake by the captives on the slave ships. On the one hand, most of the food served on the ships was low in Na+ and captives were said to receive " a little salt sometimes."(129). A common dish on board was a mixture of palm oil, flour, and horse (fava) beans called "slabber sauce." Other foods served to the captives such as rice, yams, and corn were low in salt. There are some references to "salted fish" served to slaves, although this source of Na+ was said to be mostly reserved for the crew.(48, 53). On the other hand, some 18th century contracts with English slave ships indicated that between 2 and 5 bushels of salt were loaded for every 100 slaves (130). Assuming bushels were standardized at about 56 pounds (25 kg) and the salt was pure NaCl (131), approximately 9000-21,000 mmoles of Na+ per slave would be available per journey. With an average stay on board ship of about 175 days (119 days loading and 56 days passage, (49) the daily salt intake would be about 50 to 120 mmoles of Na+ (3-7 grams of NaCl)--these relatively large salt supplies are still far less than the calculated Na+ loss during one hour under the worst conditions. Of course, conditions were not always as terrible as the scenario above and we could expect mortality of Africans to be lower on the slave ships that provided large quantities of salt to the prisoners or in whom sweating, diarrhea or vomiting were not common. Only more research in the historical archives containing documents on slave ship provisions will allow us to address more fully the issue of salt consumption on the ships.

Regardless of salt intake, under severe salt depletive conditions, "Na+ conserver" would have a decided advantage over others. If salt supplies were limited, a "Na+ conserver" would presumably have more body stores of Na+ available than others and, therefore, more protection against acute or chronic salt losses. On the other hand, if salt was readily available the daily dose would be retained longer in the "Na+ conserver" than in the others, again offering protection against acute salt losses in sweat, stools, or vomit. In both cases then, the "Na+ conserver" would have a marked survival advantage. Of course, any dietary salt would be a blessing under the conditions of the slave trade as the slave surgeon, Thomas Aubrey, noted in 1729:

"I am very sensible, that it's impossible to maintain the Slaves on Board, after one quits the Coast, without salt Provision, but then Care might be taken to water the Beef and Pork"(132).

Discussion

The nearly 400-year long trans-Atlantic slave trade was characterized by a mortality that exceeded 30%. If a genetic-based salt conserving mechanism protected some individuals from mortality then the trade might have acted as an evolutionary gate. Individuals who survived passage through that gate would possess a different genetic makeup than those who did not. This hypothetical gene(s) for Na+ conservation would, therefore, be more frequent in populations descendent from African slaves than in populations without this ancestry, (mostly residing in sub-Sahara Africa). Virtually all sub-Saharan Africans transported to the Western hemisphere between the 16th and 19th centuries, had to survive these conditions of excessive Na+ loss, and thus all passed through the same evolutionary gate. Although other population groups that migrated to the Americas during this time period were also transported across the Atlantic, their average death rate was not of this magnitude (133). In addition, no other population experienced such a death rate for such a long period of history as the African captives. The conditions of shipment of non-enslaved people were not as well standardized as they were in the slave trade and the population being transported was not preselected to be the most fit young members of the society (134). The slave trade, of course, was only the initial step in New World slavery. During the first few years in the Western hemisphere, the Africans went through a period of "seasoning"--the term "seasoned" was attributed to an individual who survived these first crucial years. Like the trans-Atlantic slave trade itself, "seasoning" was characterized by excessive sweating, diarrheas and fevers. Mortality during the first 2-4 years was an additional 15-30% (50, 13). In the second, third, and subsequent generations, the mortality rates of slaves remained very high. Major causes of death

in slave societies continued to be diarrheas and fevers, and therefore, excessive Na+ losses continued throughout the slavery period as well, (64, 135, 136). If salt supplies were also limited during this period, the mechanism of natural selection would choose those individuals most capable of salt conservation and therefore, the salt conservation trait would occur even more frequently in the second, third, and subsequent generations of Afro-Americans than among the first generation of captives. These issues will be the substance of future studies by our group.

The historical portion of this thesis also depends on a significant variation in the ability to conserve salt from the slave-producing areas of sub-Sahara Africa. One possible explanation for variability in salt conservation in West Africa lies with the ancient variations in the availability of salt (137), but it may also be related to non-renal Na+ losses from sweating and disease in sub-Sahara Africa.

Historical analysis is only the first step in this interdisciplinary project. The next step, from the epidemiological and medical disciplines, will be to conduct careful, standardized blood pressure and Na+ intake measurements among Black populations in Africa, South America, North America, and the West Indies. In addition, measurements of Na+ sensitivity, and biochemical factors influencing Na+ and water metabolism such as anti-diuretic hormone, angiotensin I angiotensin II, renin, aldosterone, atrial natriuretic peptide, kallikrein, as well as the sympathetic nervous system activity should be conducted to compare Black groups with and without ancestry from the trans-Atlantic slave trade. Finally, studies to demonstrate a genetic influence on Na+ retention in Blacks still need to be conducted.

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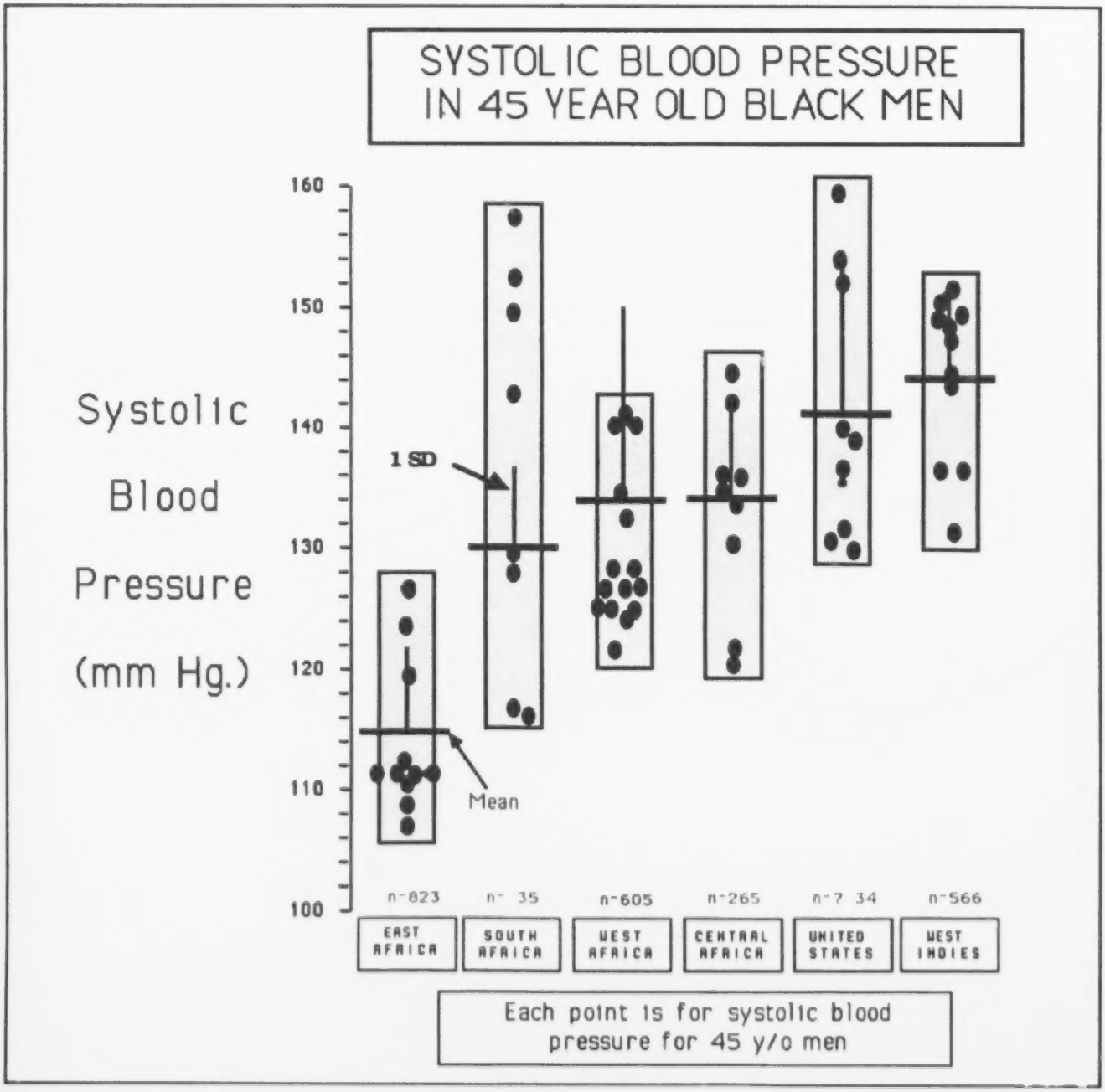

PREVALENCE AND COMPLICATIONS OF HYPERTENSION IN BLACKS

Andrew L. Dannenberg
Division of Epidemiology and Clinical Applications
National Heart, Lung, and Blood Institute
Bethesda, MD

Hypertension is a major cause of morbidity and mortality in blacks in the United States. We will review the importance of the disease and examine its prevalence and incidence in blacks. We will also present information on therapy, complications and trends in hypertension in blacks as reported in a number of studies. Finally, we will discuss new longitudinal studies currently underway which may be expected to increase our understanding of hypertension in blacks.

Importance

The National Health Interview Survey conducted by the National Center for Health Statistics has identified the chronic conditions with the highest prevalence in blacks. Hypertension is the most prevalent chronic condition seen in blacks for all ages combined. Age-specific data on prevalent chronic conditions in blacks are presented in Table 1 (1). While hypertension is only the fourth most common prevalent disease in blacks under age 45 years, it is the most common chronic condition in blacks age 45-64 years. Hypertension is second only to arthritis as the most common chronic disease in blacks age 65 years and above.

Based on data from the National Ambulatory Medical Care Survey, essential hypertension is the most common diagnosis as a cause of physician office visits for all races combined, accounting for 4.1 percent of all visits in 1985 (2). Approximately three million office visits by blacks are made annually for hypertension (3). While hypertension alone is not frequently a reason for hospitalization, it contributes to heart disease, which is one of the most common reasons for hospitalization in all races (4).

The leading causes of death in blacks are presented in Table 2. Heart disease and stroke are the first and fourth leading causes of death respectively in black males, while heart disease and stroke are the first and third leading causes of death in black females (5). Hypertension is a major contributor to both of these conditions of death.

Prevalence

The most useful data on the prevalence of hypertension in blacks are based on the second National Health and Nutrition Examination Survey (NHANES II), which was conducted in 1976-80 and included measurement of blood pressure (6). As presented in Figure 1, hypertension is slightly more prevalent in black males than black females in the younger years. After middle age it becomes more prevalent in black females. Based on a hypertension definition of systolic of at least 140 mmHg and/or diastolic of at least 90 mmHg and/or on antihypertensive medication, more than one half of all blacks over age 45 years have hypertension. Specifically, the prevalence (percent) for ages 18-24, 25-34, 35-44, 45-54, 55-64 and 65-74 years are 10.8, 23.7, 43.2, 56.2, 66.8, and 66.7 for black males respectively. The corresponding proportions for black females in those age groups are 9.4, 15.2, 36.8, 66.8, 74.3, and 82.9 (6).

Based on NHANES II data, mean systolic and

diastolic blood pressures rise with age in blacks in both males and females, as seen in Figures 2 and 3. From age 18-24 to 65-74 years, mean systolic pressure rises from 119 to 144 mmHg in black males and from 111 to 150 mmHg in black females. Across the same age range, mean diastolic pressure rises from 76 to 88 mmHg in black males and from 73 to 92 mmHg in black females (7). A rise in mean systolic and diastolic pressure with age was also observed in blacks in Muscogee County, Georgia, in 1954-55 for both sexes (8).

Considering younger persons, a rise in mean blood pressure with age has been observed among black youths age 12-17 years in the third National Health Examination Survey (1966-70) (9) and among young black adults age 18-30 years in the ongoing Coronary Artery Risk Development in Young Adults (CARDIA) Study (10).

Incidence

To monitor the public health efforts in the primary prevention of hypertension, incidence (the rate of new disease development over a time period) is a much better measure than prevalence (the proportion of population with disease at one point in time). While data on prevalence of hypertension are relatively easy to collect in cross sectional surveys, information on incidence of hypertension is more difficult to gather. Relatively few studies of blacks have included the longitudinal component necessary to define incidence in a study population. As discussed below, several new cohort studies are underway which will yield hypertension incidence rates for blacks (11-13).

One study that has provided data on hypertension incidence in blacks is the Meharry Cohort Study which followed 313 black male medical students enrolled at Meharry Medical College and initially examined between 1958 and 1965 (14-16). The mean age at examination was 27.6 years with a range of approximately 24 to 40+ years. The mean follow-up time in this cohort was 22.5 years. Hypertension in this study was defined as a blood pressure of greater than 140/90 mmHg or a history of hypertension or receiving antihypertensive medication. During the study period, 43.8 percent of the cohort became hypertensive. Thus, incidence of hypertension in this cohort can be calculated as 19.5 per year per 1000 persons (not age-adjusted) (14). The most prominent precursors of hypertension noted in this study were baseline diastolic blood pressure and weight gain (15).

A rise in hypertension incidence with age has been noted in most studies of hypertension incidence in whites (17) and among blacks in the NHANES I Epidemiologic Follow-up Study (18). However, this rise of incidence with age was not consistent among blacks in the Hypertension Detection and Follow-up Program (HDFP) in which a peak incidence was noted at age 50-59 years for both men (91.0 per year per 1000 persons) and women (66.0 per year per 1000 persons) with a decrease in incidence after that age (19). In HDFP, baseline diastolic blood pressure was a strong predictor of subsequent hypertension in blacks (19).

Treatment

The benefits of diagnosing and treating hypertension were clearly shown in HDFP (20). Five-year all-cause mortality was reduced 18.5 percent in black males and 27.8 percent in black females in comparing the stepped care (active intervention) and referred care participants in that study.

The 1988 Report of the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure includes several recommendations related to treating hypertension in blacks (21). It states that there are no recognized differences in the responses to nonpharmacologic therapy between blacks and whites and that weight reduction is strongly indicated in obese hypertensive individuals. The report notes that diuretics are more effective as monotherapy in blacks than beta blockers and angiotensin-converting enzyme inhibitors. It also states that calcium antagonists, centrally acting alpha-adrenergic agonists, peripheral alpha-blockers and labetatol are equally effective in both blacks and whites.

Based on NHANES II data, the age-adjusted proportion of persons age 18-74 years taking antihypertensive medication was 9.2 percent for black males and 19.3 percent for black females (6). From age 18-24 to age 65-74 years, this proportion rose from 0.8 percent to 23.5 percent for black males and from 1.4 percent to 58.6 percent for black females. The age-adjusted proportion of persons age 18-74 years with controlled hyperten-

sion (less than 160/95 mmHg) was 3.3 percent for black males and 11.6 percent for black females (6).

Considering only persons age 18-74 years with definite hypertension, 35.4 percent of black males and 62.9 percent of black females were taking antihypertensive medication in the NHANES II survey. Among medicated persons with definite hypertension, 35.6 percent of black males and 60.2 percent of black females had controlled hypertension (6).

Complications

Uncontrolled hypertension contributes directly to the development of nonfatal and fatal congestive heart failure and stroke. It is also a risk factor for other cardiovascular diseases and for certain kidney diseases.

Some of the best evidence of the adverse effects of hypertension on blacks comes from studies done several decades ago, prior to any substantial proportion of hypertensives receiving treatment. In a study of blacks in 1960-62 in Evans County, Georgia, subjects who had diastolic pressures of less than 90 mmHg were observed to have cardiac enlargement by X-ray at a prevalence of 37/1000 compared to a prevalence of 175/1000 for those subjects whose diastolic pressures were 100 mmHg or greater (22). Left ventricular hypertrophy by electrocardiogram in this population was observed among subjects with a diastolic pressure of less than 90 mmHg at 15/1000 compared to 76/1000 among subjects with a diastolic of 100 mmHg or greater. Proteinuria of 1+ or greater rose from 3.1 percent to 6.5 percent between these two levels of diastolic pressure. Finally, retinal vascular abnormalities of grade II (artery/vein crossing defects) or grade III (exudates, flame-shaped hemorrhages) rose from 9.3 percent among blacks with a diastolic of less than 90 mmHg to 26.7 percent among those with a diastolic of at least 100 mmHg. All of these associations are likely related to the increased blood pressure observed. However, other causes such as atherosclerosis may have contributed to some of these findings.

Hypertension is a major contributor to hospitalization for many types of cardiovascular disease. According to the National Hospital Discharge Survey which examined the first listed diagnoses in hospitalizations, among non-whites there were 625,000 hospital discharges for all cardiovascular disease in 1986, including 70,000 discharges for congestive heart failure and 109,000 discharges for cerebrovascular disease (23). Approximately 80 percent of the non-whites in this survey were black. The average length of hospital stay for non-whites with congestive heart failure was 8.7 days and for non-whites with cerebrovascular disease, was 11.2 days in 1986.

Among black males in Evans County age 40-64 years in 1960, twenty year mortality rose with increasing baseline systolic pressure for all causes, for cardiovascular diseases and for ischemic heart disease (24). Similar increased all-cause mortality and cerebrovascular disease mortality with increasing baseline diastolic pressure was observed among black males age 35-57 years in the Multiple Risk Factor Intervention Trial, based on five years of follow-up (25).

Data for overall mortality among U.S. blacks are presented in Table 3 for 1983. The 127,911 deaths of black males included 3,554 deaths due to hypertensive heart disease, 1,649 deaths due to congestive heart failure and 8,139 deaths due to cerebrovascular disease (26). As a major contributor to these causes of death as well as to other types of cardiovascular deaths, hypertension is a major contributor to a large proportion of all deaths in black males. In the corresponding 1983 mortality data for black females (Table 3), cardiovascular deaths represent an even higher proportion of all deaths.

Trends in Prevalence and Sequelae

Figures 2 and 3 are based on age-specific data from NHANES II and from the first National Health Examination Survey (NHES I) which was conducted in 1960-62 (7). Significant improvement in mean systolic pressure for blacks from 1960-62 to 1976-80 is evident for both males and females. However, relatively little change in mean diastolic pressure in blacks over this time period was observed in these surveys.

Among black adults age 25 to 74 years of age, the proportion of persons with definite hypertension decreased from 31.8 percent to 28.3 percent in black males and was unchanged at 39.8 percent in black females from 1960 to 1980 (Table 4) (27). Among those with hypertension, the proportion

of persons with undiagnosed hypertension decreased 49 percent in black males and 59 percent in black females.

It is not surprising that the proportion of hypertension which remains undiagnosed has markedly declined over the past several decades, while the prevalence of hypertension in blacks has not substantially changed. Most public health efforts related to hypertension in the 1960s and 1970s focused on the identification and treatment of persons with the disease, that is, secondary prevention of the sequelae of hypertension by lowering elevated blood pressure. Efforts to prevent the initial occurrence of elevated blood pressure (primary prevention) are beginning to receive more attention only recently.

The proportion of U.S. blacks taking medication among those with hypertension has increased over the past several decades. Comparing the two national surveys in Table 4, the proportion of hypertensive persons taking such medication rose from 18.5 percent to 40.9 percent for black males and from 48.1 percent to 60.6 percent for black females over the time period 1960 to 1980. The proportion of blacks with hypertension achieving control of their hypertension increased substantially over that time period (Table 4), when controlled hypertension is defined as on medication and a blood pressure of less than 160/95 mmHg (27). The proportion with controlled hypertension is much less when control is defined as less than 140/90 mmHg (7).

One study from North Carolina analyzed mortality trends based on all mentions of hypertension on the death certificate rather than limited to underlying cause (28). These data indicate that from 1968 to 1977 the age-adjusted death rate for all mentions of hypertension on death certificates in North Carolina decreased 19.4 percent among non-white males and 24.1 percent among non-white females. During this same time period, the death rate for ischemic heart disease as an underlying cause of death decreased 8.1 percent among non-white males and 21.5 percent among non-white females. Death rates for stroke as an underlying cause of death decreased 32.6 percent among non-white males and 31.3 percent among non-white females. Similar declines in mortality rates in blacks from 1969-71 to 1979-81 have been reported for California for all hypertension-related mortality, for ischemic heart disease, and for cerebrovascular disease (29).

National trends reflecting a decline in heart disease and stroke over the past several decades are consistent with these data (30). Age-adjusted death rate per 100,000 from cerebrovascular disease in U.S. blacks decreased from 135.1 in 1968 to 62.9 in 1984 in black males and from 118.3 in 1968 to 51.8 in 1984 in black females (31). Although hypertension-related morbidity and mortality has been substantially declining over the past several decades, elevated blood pressure remains one of the most important modifiable risk factors for death among blacks in the United States.

New Studies Underway

Several major multicenter cohort studies sponsored by the National Institutes of Health are currently underway which are likely to provide substantial new understanding of hypertension and other cardiovascular diseases in blacks. As listed in Table 5, these three longitudinal studies span the age spectrum from young adult to the elderly.

Sponsored by the National Heart, Lung, and Blood Institute (NHLBI), the Coronary Artery Risk Development in Young Adults (CARDIA) Study is evaluating young adults age 18-30 years. Slightly more than one half of the 5100 participants are black. Participants were stratified at each of the four field centers by sex, race, age, and level of education. Recruitment and the first two periodic examinations have been completed. Initial cross-sectional results from CARDIA will be published in the near future (10,11).

The Atherosclerosis Risk in Communities (ARIC) Study is an NHLBI sponsored investigation of approximately 16,000 men and women age 45-64 years in four U.S. communities (12). All participants in the Jackson, Mississippi, field center are black, while the racial composition of the cohorts in the other three field centers is representative of those communities. Recruitment and examination of the cohort in ARIC is now approximately one-half complete. Data collection in ARIC includes a physical examination related to cardiovascular risk factors and special laboratory measures of lipids and clotting factors. In addition, atherosclerosis in the carotid and popliteal

arteries is being measured, using B-scan and Dopler ultrasound, which permit direct observation of the atherosclerotic process in this large cohort.

Finally, Established Populations for the Epidemiologic Study of the Elderly (EPESE) is a study of health and chronic disease in the elderly sponsored by the National Institute on Aging. There are four field centers in the EPESE Study. Approximately one half of the study participants at the north central North Carolina field center are black. The first cycle of examinations and interviews in EPESE is now complete and some data have been published (13).

Summary

In summary, hypertension is the most prevalent chronic disease in blacks. It contributes to substantial morbidity, including ischemic heart disease, congestive heart failure and stroke. It contributes to fatal heart disease and strokes, which are respectively the first and third leading causes of death in blacks when both sexes are combined.

Secondary prevention of hypertension in blacks which involves disease identification and treatment has markedly improved over the past several decades. However, much remains to be done. New longitudinal studies involving large cohorts of blacks are underway which will extend our knowledge of the causes of hypertension.

The eventual public health goal should be the primary prevention of hypertension and its sequelae. Modifications in lifestyle are likely to be essential to accomplish this goal. Improved nutrition may be one of the most important lifestyle changes necessary to prevent the development of hypertension.

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Table 1
Prevalence per 1000 persons of most common chronic conditions in blacks by age, United States, 1984

< 45 years		45-64 years		65+ years	
Condition	Prevalence	Condition	Prevalence	Condition	Prevalence
Sinusitis	84.7	Hypertension	42	Arthritis	581.1
Hay fever	69.8	Arthritis	317.0	Hypertension	524.7
Deformity	65.5	Sinusitis	203.3	Heart disease	254.8
Hypertension	53.7	Deformity	183.6	Diabetes	220.4
Asthma	35.2	Heart disease	129.9	Hearing	220.0

Source: Reference 1

Table 2
Leading causes of death in blacks, United States, 1985

Males			Females		
Rank	Cause of Death	Rate/100,000	Rank	Cause of death	Rate/100,000
1	Heart disease	285.0	1	Heart disease	248.1
2	Cancer	212.2	2	Cancer	143.9
3	Accidents	64.0	3	Stroke	68.0
4	Stroke	58.5	4	Diabetes	25.5
5	Homicide	48.4	5	Accidents	22.7

Source: Reference 5

Table 3
Number of deaths from selected causes in blacks
United States, 1983

Cause of death	Males		Females	
	Number	Percent	Number	Percent
All causes	127,911	100.0	105,213	100.0
All cardiovascular diseases (ICD 390-448)	48,812	38.2	49,708	47.2
Hypertensive disease (ICD 401-404)	3,554	2.8	4,053	3.9
Ischemic heart disease (ICD 410-414)	21,911	17.1	20,840	19.8
Heart failure (ICD 428)	1,649	1.3	1,912	1.8
Cerebrovascular diseases (ICD 430-438)	8,139	6.4	10,423	9.9
Other cardiovascular diseases (ICD 390-448 minus above)	13,559	10.6	12,480	11.9

Source: Reference 26

Table 4
Trends in age-adjusted hypertension prevalence, diagnosis, treatment and control in black adults, age 25-74 years United States, 1960-62 to 1976-80

	NHES I (1960-62)		NHANES II (1976-80)	
	Males	Females	Males	Females
Percent with definite hypertension*	31.8	39.8	28.3	39.8
Among those with hypertension:				
Percent with undiagnosed hypertension	70.5	35.1	35.7	14.5
Percent taking anti-hypertensive medication	18.5	48.1	40.9	60.6
Percent with controlled hypertension**	5.0	20.2	16.1	38.3

* Elevated blood pressure: Systolic >= 160 mmHg and/or diastolic >= 95 mmHg and/or on medication
** Controlled hypertension: On medication and blood pressure < 160/95 mmHg

Source: Reference 27

Table 5
New multicenter cohort studies sponsored by the National Institutes of Health

Name of study*	Reference	Age	Number of participants	Number of black participants	Recruitment dates
CARDIA	(11)	18-30	5,100	2,600	1985-86
ARIC	(12)	45-64	16,000**	5,000**	1986-89
EPESE	(13)	65+	14,500	2,800	1982-86

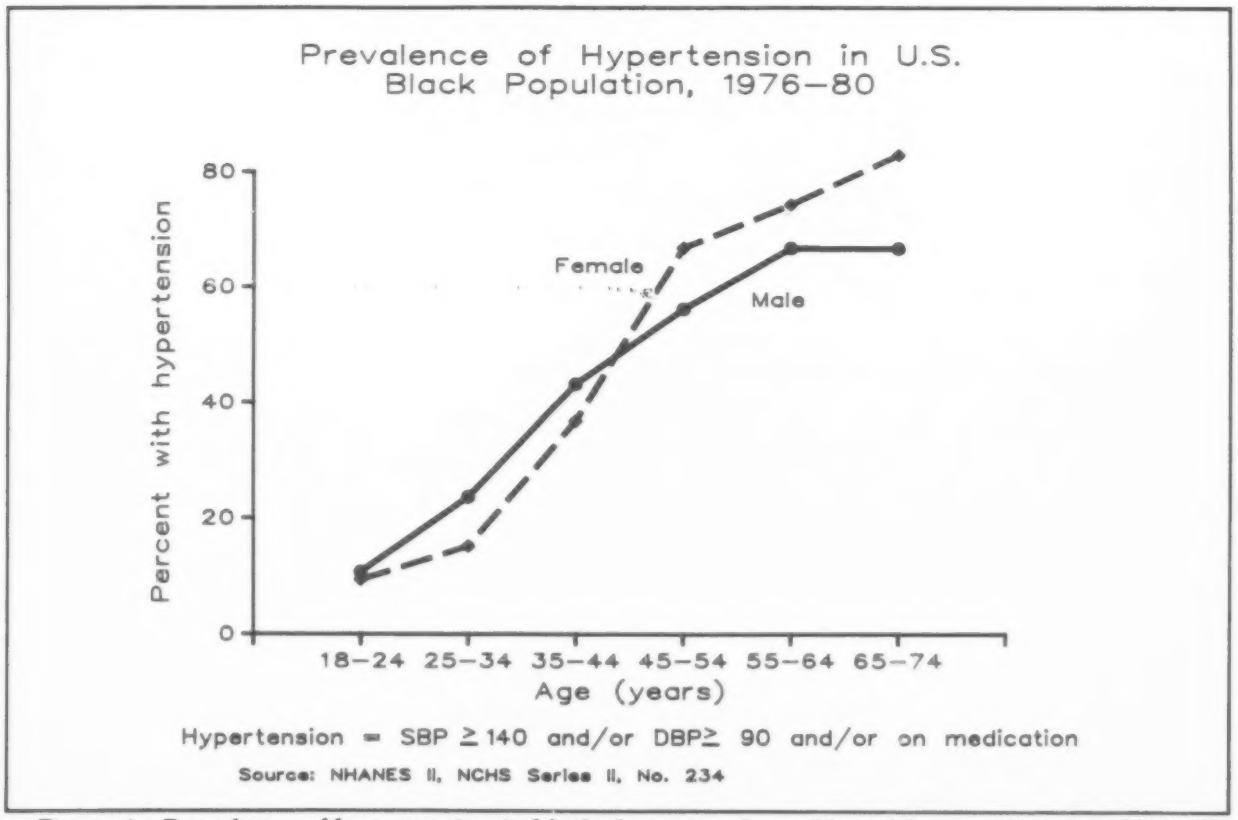

Figure 1. Prevalence of hypertension in blacks by age and sex, United States, 1976-80 (NHANES II). Hypertension defined as systolic pressure 140 mmHg or greater and/or diastolic pressure 90 mmHg or greater and/or on medication.
Source: Reference (6).

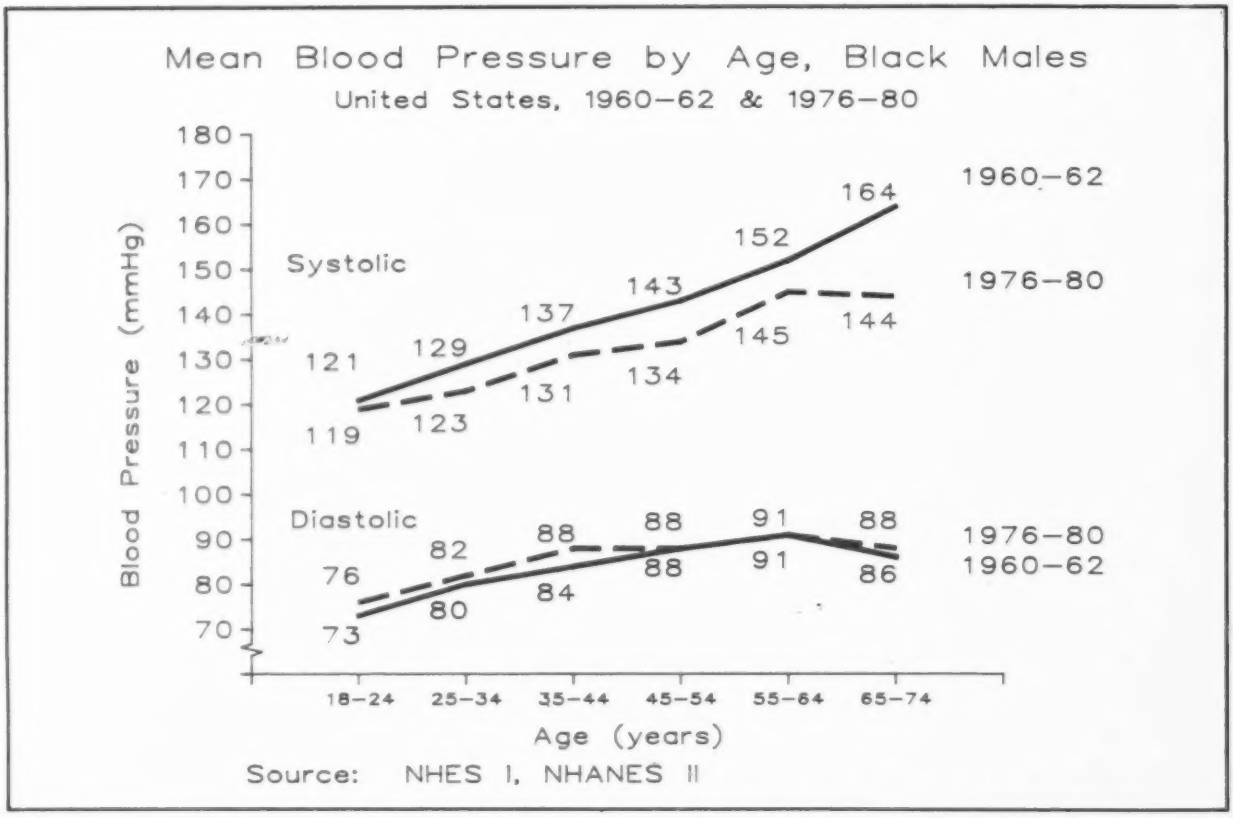

Figure 2. Mean blood pressure in black males by age, United States, 1960-62 (NHES I) and 1976-80 (NHANES II).
Source: Reference (7)

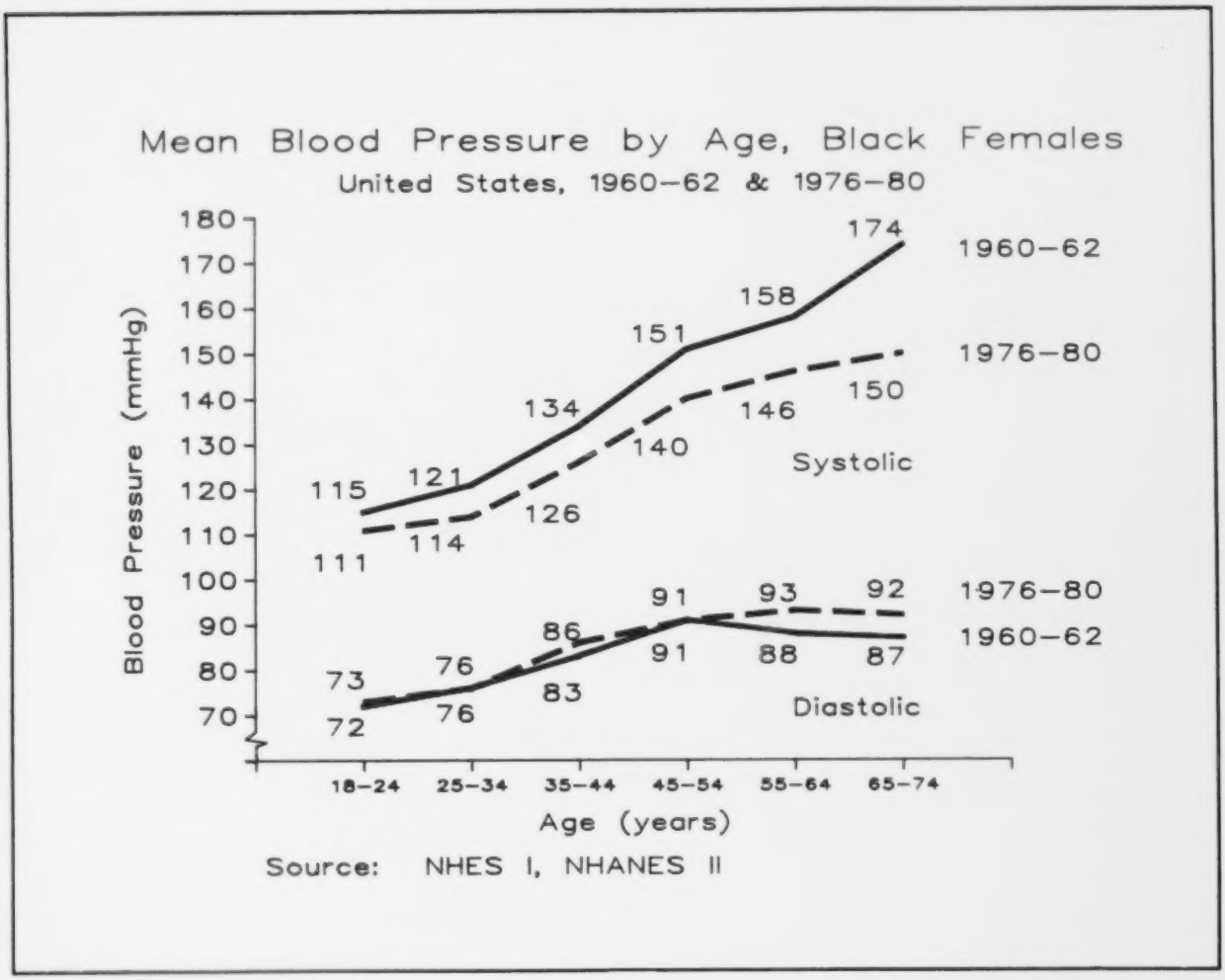

Figure 3. Mean blood pressure in black females by age, United States, 1960-62 (NHES I) and 1976-80 (NHANES II).
Source: Reference (7).

HYPERTENSION AND NUTRITION IN AMERICAN INDIANS AND ALASKA NATIVES

Brenda A. Broussard*, Sarah E. Valway
and Dorothy Gohdes
Indian Health Service Diabetes Program
2401 12th Street, N.W., Room 211N
Albuquerque, NM

Introduction

In 1955, the Indian Health Service, an agency of the United States Public Health Service, was established to improve the health status of American Indians. Since then, significant improvement in mortality has been achieved (1) (Table 1). With the control of infectious diseases such as tuberculosis and gastroenteritis, chronic diseases have emerged in importance.

In an extensive review of the diseases in North American Indians, Sievers and Fisher presented data showing the increase in acute myocardial infarctions in certain Southwestern Indian tribes (2). Although the mortality rate for heart disease among American Indians and Alaska Natives was less than the rate for the United States, heart disease was the leading cause of death from 1983-1985 (1). In addition, non-insulin-dependent diabetes mellitus (NIDDM) has become a major health problem in contemporary Indian communities (3). Epidemiologic studies suggest that this health problem is linked to increasing obesity (4). Although hypertension and obesity are correlated in many populations, there are little data about hypertension in Indians. Scattered reports describe the prevalance of hypertension in different tribal groups, but no one report has described the prevalence of hypertension in these disparate groups at the same time (5-9). This paper presents the prevalence of clinically diagnosed hypertension in 1985 among American Indian and Alaska Native patients served by Indian Health Service facilities and reviews data about hypertension and nutritional factors that may be associated with hypertension in selected Indian groups.

Methods

The Indian Health Service and its tribal contractors collect clinical and demographic information for each outpatient encounter. Facilities are grouped into areas shown in Figure 1. Most areas used an ambulatory care reporting form that allows the provider to make two choices among disease categories and descriptions of care, i.e., hypertension, physical examination. Alaska, Billings, and Tucson Areas used a computerized system with more flexibility. Facilities in California, New York, Rhode Island, and Maine did not use this reporting system in 1985.

Data from the ambulatory visits were aggregated by the Indian Health Service Data Processing Center for the period of October 1, 1984 to September 30, 1985. Records with a diagnosis of hypertension were sorted by facility, patient record number, and date of service. When records indicated the same facility code and patient record number, only the latest visit was used for further analysis. Records were then sorted by sex, community of residence, date of birth, and date of service. The record with the latest date of service was selected when duplicate records were found. This procedure ensured that individuals who might have received services in several regional facilities were counted only once. The records were then sorted by residence and age group.

Rates were computed using the 1985 IHS pro-

*Speaker

jected population and were adjusted to the U.S. 1980 population (10). Age distributions for Indians in each service area were estimated from the age distributions of Indians residing in the state which encompassed the major part of the service area.

Results

The 1985 estimated age-adjusted prevalence of hypertension among American Indians and Alaska Natives was 745/10,000 for persons aged 15 years and older (Table 2). There was considerable variability in hypertension rates among the American Indian and Alaska Native populations. Bemidji Area had the highest rate at 1268/10,000. Phoenix, Oklahoma, Nashville, Albuquerque, and Aberdeen Areas had rates above the overall IHS rate, with rates ranging from 808 to 967/10,000. The lowest rates were in the Portland, Alaska, Navajo, Tucson, and Billings Areas with rates from 396 to 716/10,000. The Portland IHS Area may show an artificially low prevalence rate because much primary care is delivered by individual contract providers and diagnoses were not recorded in the ambulatory care data base used for these analyses. Prevalence rates of hypertension in American Indians and Alaska Natives are significantly lower than national rates for other ethnic groups in the U.S. (Table 3). American Indians and Alaska Natives have a hypertension rate approximately 60 percent that of non-Hispanic Whites and Hispanics and 42 percent that of Blacks (11).

The Midwest Region of the U.S. had the highest rates of hypertension for both IHS users and all other ethnic groups (Figure 2). In the Midwest, the rate for American Indians was 1089/10,000. American Indians and Alaska Natives in the West had a rate of 703/10,000 and those in the Northeast and South had a rate of 823/10,000. In all regions American Indians and Alaska Natives had hypertension rates significantly lower than other ethnic groups.

Discussion

This study constitutes the first systematic attempt to determine the prevalence of hypertension among American Indians and Alaska Natives. There are some limitations to the data. This study included only 12 months of data - fiscal year 1985. Due to the nature of the IHS reporting system, the data do not include contract health services. This may result in an underreporting of the rates for Bemidji, Portland, and Nashville Areas, areas with high levels of contract care use. Also, the data do not include California Indians or Indians living in urban areas who do not use IHS facilities.

The epidemiology of hypertension among American Indians and Alaska Natives is not well documented. Table 4 shows the wide variance of prevalence rates in studies conducted among American Indians and Alaska Natives over the past three decades. Prevalance rates ranged from a low of 1 percent in Southwestern Indians in 1950-1952 and 3 percent in Alaskan Eskimos in 1958 to 44 percent in Alaska Aleuts on 1966.

Nutritional factors that clearly contribute to hypertension include obesity (20 percent or more over desirable body weight) and excessive intake of sodium and alcohol (17-21). Low intake of calcium has also been suggested as a factor in hypertension (17).

In 1985, about one-fourth of all U.S. adults were obese (11). Obesity has become a major health problem for most American Indian and Alaska Native communities as well (22). A report in 1971 found that 97 percent of Pima Indian women in Arizona were obese (23). Another study of Pima Indians aged 20-34 done in 1980 found that 73-78 percent of men and women were above 120 percent of desirable weight (24). Obesity has also been described among other adult Indians - Oklahoma, Navajo, and Penobscot (6,25,26). Pediatric and adolescent obesity has also become a concern in American Indian communities. A report in 1979 found 50 percent of Cherokee teenage boys at 32 percent of teenage girls ages 13-17 in North Carolina were obese (27). Data from the 1986 Pediatric Nutrition Surveillance System on American Indian and Alaska Native children under age five years showed a high prevalence of obesity, with 13 percent of children at age 2 years and 10 percent of children at age 5 years significantly overweight (28).

Various theories have been offered to explain the high prevalence of obesity in the American Indian and Alaska Native populations, namely,

increased caloric intake and a sedentary lifestyle (24). In addition, Neel's "thrifty gene" hypothesis in 1962 suggested that obesity, insulin resistance, and non-insulin dependent diabetes mellitus result from the introduction of a steady food supply to people who have evolved an ability to store energy efficiently, permitting survival under conditions of alternating periods of feasting and famine (29). In a recent study of Pima Indians, Ravussin and his colleagues found that some Indian families have particularly low metabolic rates. These subjects had a fourfold increase in the risk of gaining more than 7.5 kg weight over a two year period (30). Three studies on caloric intake in American Indians and Alaska Natives do not suggest that obesity is simply a result of excessive food consumption (26,31,32). A noted exception is a 1971 diet survey of 277 Pima Indian women which found a mean caloric intake of 3,164 kcal/day (23). Another dietary survey is presently underway in this community to determine current nutritional status.

Many studies have associated sodium intake and hypertension (33). There is a paucity of data on the intake of sodium in American Indians and Alaska Natives. The 1971 comprehensive diet survey of Pima Indians did not examine sodium intake (23). The only well-documented study in an Indian community is one reported by Welty et al. in Gila Bend Papago Indians of Arizona (16). Mean sodium intake from water and food sources was found to be 4,687 mg, similar to intakes of the neighboring non-Indian population. Interestingly, the hypertension rates were similar for all age groups.

A relationship between low dietary calcium and hypertension has been suspected for many years, but this is controversial (33-34). Again, data on calcium intake in American Indians and Alaska Natives are sparse. In nutritional studies of three Indian populations, calcium intake was below the recommended dietary allowance (23,26,32). Principal sources of calcium are nonfat dry milk and processed cheese provided by the USDA Supplemental Food Program (31). Because there is a high prevalence of lactose intolerance in the American Indian and Alaska Native populations, it is not surprising that calcium intake is low (35).

Another possible factor contributing to hypertension is alcohol. Alcoholism has become a major health problem among American Indians and Alaska Natives, and is an underling factor in several of the leading causes of death. In 1985, over 20,000 American Indians and Alaska Natives were treated for alcoholism and substance abuse (1). The association of alcohol with hypertension is well recognized and has been described in Navajo Indians (8). No data are available presently for other tribes.

The data on hypertension prevalence in American Indians and Alaska Natives suggest more questions than answers:

. Is the prevalence of hypertension increasing in American Indians and Alaska Natives?

. What factor(s) contribute to the wide variance seen in the prevalence of hypertension across tribal groups?

. What effect does the increasing rate of overweight in American Indians and Alaska Native have on the prevalence of hypertension?

. What effects do sodium, calcium, and alcohol intake have on hypertension in American Indians and Alaska Natives?

Obesity is a significant health problem in these communities. Obesity-related diabetes, i.e., NIDDM, has become epidemic in many Indian groups (3). The known relationship of obesity to hypertension suggests that this population should also have high rates of hypertension. Yet our data reveal the converse. The relative contribution of obesity to hypertension in American Indians and Alaska Natives has not been studied. Neither has there been any longitudinal study of hypertension in this population to document trends in rates. The variance in hypertension among different tribes is striking and the reasons for this are unknown.

Acknowledgements:

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Table 1
Program Accomplishments since
Indian Health Service established (1955)*

	% Decrease in Mortality through 1983-85
Infants	84
Under 28 Days	80
28 Days - 11 Months	87
Maternal	87
Pneumonia and Influenza	82
Gastrointestinal	93
Accidents	51
Certain Diseases Orginating in the Perinatal Period	87
Tuberculosis, All Forms	97
Congenital Malformations	66

*Source: USDHHS, PHS, IHS Chart Series Book, April 1988, Chart 5.1.

Table 2
Age-Adjusted Rates of Hypertension by IHS Areas - 1985
Per 10,000 Population*

IHS Service Area	Rate
Bemidji	1268.3
Aberdeen	966.9
Albuquerque	895.3
Nashville	842.7
Oklahoma	818.8
Phoenix	808.1
Billings	715.7
Tucson	649.8
Navajo	593.3
Alaska	542.8
Portland	396.2
All IHS Areas	744.8

*15 years of age and older
+Age-adjusted to 1980 United States all races population.

Table 3
Comparative Age-Adjusted Hypertension Rates*
in Selected Populations
Per 10,000 - 1985

Black[1]	1756.0
Hispanic[1]	1266.5
White[1]	1236.6
American Indian/ Alaska Native[2]	744.8

National Health Interview Survey, National Center for Health Statistics, Age 18+.
[1]1985
[2]IHS Users. Direct Patient Care Statistics, IHS, 1985, Ages 15+.
*Age-adjusted to 1980 United States all races population.

Table 4
Hypertension Prevalence (%) in Several
American Indian/Alaska Native Populations

	Prevalence (%)	Refs
Western Indians 1950-1952	1	12
Alaskan Eskimos 1958	3	13
Apaches 1958	31	14
Navajos 1956-1962	4	15
Navajos 1977	17	8
Alaskan Aleuts 1966	44	7
Alaskan Aleuts 1976	27	7
Papagos 1969-1972	20	9
Papagos 1983	23	16
Penobscot 1981	23	6
Urban Minnesota	15	5

STRESS-NUTRITION INTERACTIONS AND BLOOD PRESSURE

Frederick A. Ernst
Cyril O. Enwonwu and Rupert A. Francis
Department of Family and Preventive Medicine
and Center for Nutrition
Meharry Medical College
Nashville, TN

Introduction

It is well known to behavioral scientists that an enormous literature has amassed concerning the effects of stress on blood pressure and its probable role in the development of essential hypertension (1, 2). Similarly, nutritional scientists have witnessed comparable quantities of research reports addressing the effects of various nutrients on blood pressure and hypertension (3-6). Interestingly, however, relatively few studies have focused on the interactive effects of stress and nutrition on the cardiovascular system. This is particularly true when a search of the literature is restricted to human studies. The purpose of this paper is to briefly review several of the studies in which stress and nutrition were addressed concomitantly with specific regard to human blood pressure. As well, we intend to present the results of preliminary studies, still in midstream, which we are performing here at Meharry to address this important problem among blacks.

It seems quite clear from an examination of the available literature that an important obstacle to a combined research focus derives from the historical difficulties of behavioral scientists in arriving at a generally accepted operational definition of human stress (7-8). Because of the methodological problems arising from the lack of consistent definitional clarity and utility, some serious researchers have even recommended that the term, "stress," be abandoned (9).

However, there has emerged in recent years an interesting and productive alternative in the approach to understanding the influence of environmental demands (read, stress) on the cardiovascular system and, perhaps, on health in general. This new approach has shifted the focus to the response side of the traditional S-R model of behavioral psychology. Variability in human response to a standardizable uniform environmental challenge may well reveal more useful information about cardiovascular function (and vulnerability) than the perseveration of futile efforts to quantify stress as a universally understood stimulus. Simply put, "how we react may be much more revealing than what we are reacting to." It is in this context that cardiovascular reactivity testing has begun to enjoy increasing acceptance as an important instrument for research concerning stress and heart disease (10).

In the other arena, nutritional scientists have enjoyed the luxury of relatively more quantifiable parameters in their investigations of nutrition and cardiovascular disease. For example, an abundance of research has addressed the connections between salt and hypertension in part due to the extent to which sodium intake and outflow are amenable to quantification and readily interpretable in physiologically intact subjects. However, despite the advantages of methodological precision and data interpretability, there is no more a concensus among nutritional scientists concerning the influence of salt on heart disease than there is among behavioral scientists concerning stress and heart disease.

However, it is possible that no single nutrition-

al or behavioral factor is capable of exerting a truly pervasive influence on pathophysiologic processes except perhaps under very unusual or extreme circumstances. On the other hand, it is plausible that multiple nutritional factors may act synergistically with one or more behavioral factors to produce a truly appreciable influence on physiological functioning, and ultimately disease outcome. Indeed, we are confident that by the end of this century, significant gains in our understanding of heart disease will have been accomplished from increasing investigations of interacting nutritional and behavioral factors.

Before presenting the preliminary results of our contribution to this effort, an examination of landmark research and a few related investigations is warranted. Earlier in this decade, Light and Falkner (11,12) and their colleagues reported that the stress of performing a series of competitive mental tasks precipitated sodium and water retention in a group of young men who were at risk of hypertension by virtue of positive parental histories or borderline blood pressures. Following salt loading (10 gm/day sodium chloride), subjects with positive parental histories of hypertension had greater reactivity of systolic (SBP) and diastolic (DBP) blood pressures to mental challenge.

Studies of this sort have only recently turned their attention to blacks despite the facts that blacks are thought to have greater genetic vulnerability to hypertension (13), have higher resting blood pressures than whites (14), are more likely to be salt sensitive (15), and are unquestionably disproportionately affected by hypertension (16).

A group of investigators at Duke, for example, demonstrated that blacks show larger changes than whites in SBP, DBP, and peripheral vascular resistance to a cold facial stimulus (17). This is a particularly important finding because the procedure they employed is thought to differentially elicit a-adenoreceptor sensitivity. And, of course, activity of the a-adrenergic system is largely dependent on the neurotransmitter, norepinephrine, which is a product of the amino acid, tyrosine. Summarily, their findings suggest a proneness in blacks to blood pressure elevations tied more to vascular resistance than to cardiac output. This is consistent with other studies suggesting racial differences in sensitivity to norepinephrine (linked also to sodium sensitivity) (18) and the resistance of black hypertensives to antihypertensive therapy based on a-adrenergic blockade (19).

The group at Duke also recently reported an interesting finding concerning cardiovascular reactivity in young black women (20). Subjects with parental histories of hypertension actually showed smaller cardiovascular changes to a stressful task when compared to same-aged women with no parental histories of hypertension. This is opposite to what has been found in whites. However, it should be noted that only females were used in their analyses and their ages ranged only within 18-22. The overall mean for age was not reported but appeared to be less than 20. Both sex and age have been demonstrated to exert distinct influences on cardiovascular reactivity and their paradoxical findings might well have been a simple product of using very young females. Moreover, in their study comparing cardiovascular responses to cold facial stimuli in black and white males, their ten black subjects weighed only an average of 147 pounds. and were not older than 21. Even the white subjects in their study weighed an average of only 160 pounds. As a whole, their subjects were decidedly lean, and perhaps decidedly healthy! These are important factors to consider in light of the observation that blacks do not show significant changes in blood pressure until around age 25 (21) and because of findings related to age and sex in general, already cited above.

Another relatively recent study by Fredrikson (22) examined racial differences in cardiovascular reactivity to a reaction-time task in which an aversive auditory stimulus was delivered for poor performance. Whites were more reactive in measures of a-adrenergic activity (SBP and heart rate), while blacks showed more vascular (a-adrenergic) reactivity. Since his study also compared normotensives with borderline and established hypertensives, his subjects were significantly older (means were 41-52) than those of the Duke group, and this creates some difficulty in comparing the findings of these important studies.

Methods and Subjects

Our research is investigating the interaction of several nutritional and behavioral factors on cardiovascular reactivity in young black males with positive (PH+) and negative (PH-) parental histories of hypertension. This presentation is a "midstream" progress report in which eighteen PH+ and PH- males have been tested for cardiovascular reactivity following five days of high (300 mEq) or low (10 mEq) dietary sodium at two levels of dietary calcium intake (1100 mg and 550 mg/day). Other nutrients (e.g., potassium and magnesium) which are believed to affect cardiovascular activity were controlled at RDA levels. The eighteen subjects were a mixture of medical students, other college undergraduate students, and young men in the community who heard of our studies through friends or acquaintances at Meharry. Their average age was 23.6 years. They had mean heights of 71.25 inches and weights of 186.8 pounds. (See Table 2 for additional descriptive statistics.) All subjects completed questionnaires to assess certain dietary preferences, as well as tobacco, alcohol, and caffeine use. They were also administered a questionnaire which included a brief measure of anger designed by the investigators as well as the Cook-Medley, Hostility, Overcontrolled Hostility, and Hy5 scales of the MMPI.

Procedures

Dietary control was achieved by providing a monetary incentive for subjects to eat all meals for five consecutive days in our clinical research center. Twenty-four hour urine collections provided data concerning baseline sodium, potassium, calcium, and magnesium excretion. Repeated urine chemistries were used to verify dietary compliance. During the five day dietary protocol, cardiovascular measurements (systolic, diastolic, mean arterial pressures, and heart rate) were obtained prior to each meal in a sitting position following five minutes of rest. On the final day of the diet, subjects were tested for cardiovascular reactivity utilizing a protocol developed in our laboratories. Table 3 presents 24-urine chemistries for our two main comparison groups.

The rationale for using mentally challenging tasks to assess cardiovascular reactivity rests on the premise that specific patterns of reactivity, particularly hyperreactivity (sometimes called hyperkinetic cardiovascular response) can be identified as an early possible index of vulnerability to cardiovascular disease. An analogy might be drawn here to the cardiologist's use of the treadmill, also a type of stress test. It is frequently used to reveal an underlying heart disease which would not be apparent under resting circumstances. In the "psychophysiological" stress test, it is important for the specific challenging task to elicit reactivity which reliably differentiates relatively vulnerable from relatively resistant subjects. In so doing, the test is considered "sensitive."

Our version of cardiovascular reactivity testing has three mentally challenging features. First, the core element of the test is the Stroop color-word conflict task, in which we present one stimulus at a time on a computer screen. The task consists of responding to the words, RED, BLUE, or GREEN, as they are presented on the computer screen. Subjects are asked to read the stimulus word when it appears in black and name the color of the word if it appears in a color (red, blue, or green - which never corresponds to the stimulus word). The task causes cognitive conflict between two responses learned typically very early in life, that is, reading and color naming. Second, the word stimuli are presented at two-second intervals to create time pressure. And third, headphones placed over the subject's ears carry prerecorded randomly-ordered repetitions of the words, RED, BLUE, and GREEN so as to create task interference which the subject must contend with if he is to successfully negotiate the task. While virtually all subjects adapt to the task in time, the cardiovascular activity concomitant with the adjustment provides the data upon which interpretations can be made concerning the subject's nutritional status, parental history, or other potential indices of vulnerability. An important feature of our protocol is the use of three specific presentations of the task, each of three minutes duration, separated by two minute rest intervals. Five minute periods of rest precede and conclude the test protocol. These important features permit an analysis of response adaptation (or perseveration) which may reveal a more subtle manifestation of cardiovascular vulnerability than one based on a single reactivity measure so frequently encountered in the litera-

ture (typically magnitude of cardiovascular change).

The sensitivity of our test has been documented by reliably differentiating subjects with and without cardiovascular disease. For example, an interesting single case study is found in a 46 year old white male executive who had a history of cardiac arrhythmia (PVC's) following coronary bypass surgery. His PVC's were not well controlled by a conventional regimen of propranolol. Sample strips of his EKG during the administration of the reactivity test are illustrated in Figure 1. Dramatic changes in the frequency of PVC's can be seen as he anticipated the beginning of the first task trial (labeled PREP), and a further exacerbation of the arrythmia can be seen during the first thirty seconds of the task (labeled STRESS). Note that runs of ventricular tachycardia appear in this strip. A summary of his response to the various segments of the test is presented in Table 1. Adaptation can be seen in the decrease of PVC's across the repetitions of the task (Stress 1 to Stress 2 to Stress 3). Interestingly, his cardiologist reported significantly less PVC activity during a treadmill EKG performed little more than a week previous to this testing. Clearly, for some, mental demands have had better track records as elicitors of pathophysiological reactivity and as differentiators of at-risk groups than physical demands (e.g., cold pressor test (23)).

Previous Results

An early version of our protocol was used to test 195 subjects, of whom 46 were hypertensives in various stages of step-care antihypertensive medical treatment. The reactivity data of this group of hypertensives contrast informatively with those of 149 normotensives. Analyses were performed on the distributions of blood pressure changes calculated as the difference between baseline (resting) BP's and the BP's during the first of three challenges on the mental task for 149 normotensives and 46 hypertensives. This difference score will hereafter be referred to as BP-delta. Analysis of variance reveals a highly significant difference in systolic blood pressure reactivity between normotensives (Mean = 18.5) and hypertensive (Mean = 25.2) subjects (F=13.02, P = .001). Differences in diastolic blood pressure reactivity (Means = 10.1 and 12.0 respectively) are marginally significant (F = 2.93, P = .075). Figure 2 illustrates these differences. It is also significant that more than 45 percent of hypertensive subjects react with a minimum of 30 mmHg SBP-delta, while only 15.4 percent of normotensives meet or exceed the 30 mmHg criterion. Chi square analysis with Yates correction for continuity reveals that the differences in these percentages are highly reliable ($X^2 = 6.06$, P = .0134). And finally, 6 of 46 (13 percent) of hypertensive meet or exceed the criteria for both SBP and DBP simultaneously, while only 3 or 149 normotensives do ($X^2 = 8.67$, P=.0037). Figure 3 illustrates these differences.

Hypotheses

These data are presented as evidence of the sensitivity of our test to reveal differences between individuals with contrasting cardiovascular status. The eighteen subjects we have tested thus far are providing data to assess the ability of our test to reveal differences in cardiovascular activity as a function of dietary sodium and calcium and parental history of essential hypertension. We are proposing several hypotheses concerning the interaction of behavioral and nutritional factors:

1. Excessive dietary sodium increases resting blood pressure.
2. Levels of resting blood pressure are higher in subjects with parental histories of hypertension.
3. Excessive dietary sodium produces larger increases of resting blood pressure in subjects with parental histories of hypertension.
4. The effect of excessive dietary sodium on blood pressure is potentiated under conditions of mental challenge.
5. The effect of parental history on blood pressure is potentiated under conditions of mental challenge.
6. The effect of sodium on blood pressure is attenuated by other interacting dietary nutrients.

Results and Discussion

Although data collection to fully test these two hypotheses is currently incomplete, some interesting preliminary findings have begun to emerge. For example, we examined cardiovascular data collected before breakfast for each of the five days (prebreakfast measures are preferred to

lunch or dinner, since there is less variability in blood pressure earlier in the day, i.e., prior to physical activity, other environmental demands, etc.). Using a repeated measure MANOVA, the effects of parental history and dietary sodium were analyzed for the five consecutive (repeated) measurements. Figure 4 reveals an adaptation of SBP across the five day period for all subjects combined. The progressive decreases were statistically reliable (P = .039) and certainly not unexpected. However, when the two levels of dietary sodium were examined, somewhat differing patterns of adaptation emerged (Figure 5). The high sodium subjects appeared to have achieved greater SBP adaptation than the low sodium subjects despite starting at almost identical First Day levels. This difference from Day 1 to Day 5 proved to be statistically significant (P = .03). While it is true that all high sodium subjects at this stage of our data collection are also high calcium subjects, the finding is still somewhat remarkable. That is, one can only conclude that either the high sodium did not have its expected effect on blood pressure or, perhaps more interestingly, its effect was neutralized by the concomitant high calcium. While either conclusion is palatable and an interesting finding in its own right, a differentiation must await further data collection.

Figure 6 illustrates the change in SBP for the two parental history groups. As expected, PH+ subjects showed markedly greater perseveration of SBP reactivity when compared to PH- subjects, as clearly depicted in Figure 8. This difference proved to be reliable (P = .049). An analysis of the segment in which the perseveration occurred yielded a highly reliable difference between PH+ and PH- subjects (P = .035). Indeed, this neatly illustrates the need for repeated exposure to the stressor when cardiovascular reactivity is assessed. The differences between these two groups would not have been apparent if simple magnitude of change were the only dependent measure differentiating the vulnerability of these two groups.

So far, we have found no reliable differences in reactivity of DBP or mean arterial pressure (MAP) in either of the two primary group comparisons. However, HR reactivity proved to be greater in both the PH- (P = .08) and the low sodium subjects (P = .059). This partially replicates the observations of Falkner, et al. (11) and appears consistent with Anderson's data (17), in which PH+ subjects had lower pretask baseline HR's and lower HR's to the demands of the task. There is also an appearance of lower HR in subjects with the largest quantity of salt-loading in data reported by Luft, et al. (24).

A most interesting finding in our admittedly preliminary results relates to several observations in connection with calcium. For example, correlational analyses of 24-hour urinary calcium on the fourth day of dietary control revealed a powerful inverse relationship between urinary calcium and SBP reactivity (r = -.49, P = .05). No such relationships were found between SBP reactivity and sodium, potassium, or magnesium (see Table 4). Neither did the amount of urinary calcium differ in the two sodium conditions (t = 0.43, P = .67) nor the parental history groups (t=0.90, P=.38), so that the relationship between urinary calcium and SBP reactivity appeared to be very specific. An interpretation of this finding is difficult at this stage of our data collection. However, one might conclude that a negative correlation between urinary calcium and SBP reactivity was found because those subjects with adequate calcium status are more likely to excrete larger (unneeded) ingested calcium, and either their chronically higher levels of dietary calcium or their efficient utilization of ingested calcium has an attenuating or prophylactic effect on the reactivity of blood pressure to stress. Put another way, those who would need less calcium (by virtue of their adequate calcium status) are more likely to excrete more ingested calcium, and having sufficient intake levels of calcium is somehow protective. In interpreting our data, it is also important to recognize that the low calcium subjects did receive 550 mg/day, which might be regarded by some as marginal, especially in the short run.

Most surprisingly, our data do not support the hypothesis that excessive dietary sodium increases blood pressure in normotensive young black males, including those with positive parental histories of hypertension. While our study employed a rather brief dietary protocol, it is nonetheless interesting that our subjects were not differentially reactive despite being considered vulnerable because of racial and/or genetic factors.

Analysis of individual response curves of daily resting blood pressures revealed no evidence of reactivity to excessive dietary sodium in any one of the subjects. Certainly at least one of the more obese subjects with a positive parental history of hypertension would be expected to show some increase in daily resting blood pressure during five days of a 300 mEq dietary sodium load! Three plausible explanations concerning the absence of reactivity can be entertained, recognizing that conclusions cannot be confidently drawn from "negative results." First, our subjects were young and presumably healthy at the time of participation in the study. There is no reason to believe that blood pressure should necessarily be affected by short-term excessive dietary sodium in young people who have no evidence of cardiovascular or renal disease. Second, as indicated above, sodium sensitivity might have been attenuated by the high level of dietary calcium employed in our protocol. Other studies investigating sodium sensitivity have typically employed concomitant dietary calcium at amounts considerably less than RDA levels (e.g., 17). Third, and perhaps most important, "sodium load" in studies of sodium sensitivity is typically achieved by adding large amounts of NaCl to an otherwise balanced diet. Only 0.5 gm/day of NaCl contributed to our 300 mEq sodium diet, while it is common to find a minimum of 6 gm/day used in other studies which employ a 300 mEq sodium diet. In light of recent findings about the "salt sensitivity" of blood pressure being quite possibly tied specifically to the chloride molecule (25), studies of sodium sensitivity which employ large amounts of NaCl are currently difficult to interpret.

Our hypotheses concerning the ability of our reactivity test to differentiate dietary conditions and parental histories are at present only partially confirmed. Virtually no difference in cardiovascular reactivity was found between subjects in the two dietary conditions. For this result, we would propose the same set of interpretations as indicated above concerning the daily resting cardiovascular measures. However, one measure of our test did reliably differentiate parental history irrespective of the dietary condition. This important finding requires careful analysis.

First, there were no differences in baseline levels of systolic blood pressure, nor were there significant differences in the magnitude of change (response magnitude) in systolic blood pressure between the two parental groups. This finding was somewhat unexpected in light of the frequency with which this measure of reactivity is found to differentiate parental history in most of the existing literature (2). However, our two parental history groups were differentiated by a second measure of reactivity, one which we feel is more significant. Subjects with positive parental histories of hypertension reacted to mental challenge with changes in systolic blood pressure which resisted habituation (some might prefer the term adaptation) upon repeated application of the same challenge. We will use the term "response perseveration" to identify the phenomenon in which there is a resistance to habituation when a challenge is repeated in an identical form separated by brief uniform rest periods.

Response perseveration is a reactivity phenomenon having a more plausible role than response magnitude in the possible connection between stress and the development of stable hypertension. That is, it seems plausible that a chronic elevation of blood pressure would be more likely determined by repeated increases in blood pressure to an unchanging or generalized stressor (response perseveration) rather than a simple product of a large response magnitude to any single stressful encounter. If "resetting of the baroreceptor thermostat" for blood pressure regulation is an important pathophysiological link in the chain of events leading to hypertension, it is more plausible that perseveration of blood pressure reactivity would contribute more to the "resetting" than any other single stress-induced elevation. As such, perseveration would be a more powerful marker of vulnerability to the development of hypertension and should be included in any serious attempt to construct a cardiovascular reactivity test which would reliably predict cardiovascular disease.

Finally, we propose a theory to account for the importance of response perseveration to the role of stress in the development of essential hypertension. Habituation is thought to involve active inhibitory processes. That is, the diminution of a response to repeated stimulation is not simply

due to the gradual "death" or elimination of the response. Rather, the process of reduction to zero percent of its original magnitude is determined by inhibitory action which increases with each repetition of the original stimulus. Specifically, then, blood pressure which decreases in magnitude to repeated challenges does so because the mechanism controlling the habituation (gradual inhibition) of the response is functioning properly. On the other hand, blood pressure which resists habituation is, by definition, disregulated, and probably by virtue of some neurophysiological dysfunction. We advance a neurophysiological theory of dysfunction based on what we will call Multiple Inhibitory Demand Capacity.

It must be recalled that our reactivity test has several components. At its core is the Stroop test, which is a mentally challenging cognitive task. While our test also includes time pressure, a possibly most critical component is the auditory interference described above. The significance of this interference is that a subject must "block it out" to successfully negotiate the task. Put another way, the subject must engage in an active inhibition of attention to the interference. Subjects accomplish this with varying degrees of success but, more importantly, the task as a whole causes at least two inhibitory actions to be engaged simultaneously. We propose that the inhibitory action on blood pressure is either abandoned or "short-circuited" with simultaneous inhibition of attention to the interference. In other words, successful inhibition of one response causes a reciprocal disinhibition of a response which would otherwise have been actively inhibited at the same point in time. This, of course, assumes that there is some central control mechanism responsible for the coordination of active inhibitory regulations throughout the total system. One might argue further that various individuals have varying degrees of inhibitory capacity based on the integrity of the central control system.

Obviously, many subjects successfully negotiate multiple inhibitory demands. However, our data suggest that individuals vulnerable to hypertension by virtue of parental history have a diminished capacity to accommodate multiple inhibitory demands, as evidenced by the perseveration of blood pressure reactivity to repeated stimulation. We therefore advance the hypothesis that vulnerability to hypertension, especially stress-related hypertension, is at least partially a product of limited multiple inhibitory demand capacity. Further confirmation of our hypothesis could help to clarify the equivocal findings concerning connections between the control of anger and its effects on blood pressure. For example, it is interesting to speculate about the relevance of our theory to understanding the disproportionate frequency of hypertension in black Americans. Blacks living in America (and in Western Civilization generally) are almost exclusively descendants of slaves. Clarence Grim has already raised interesting questions about the survival of slaves who were efficient at sodium retention and the selective genetic effects created for subsequent generations. We would add that further survival might also depend upon the development of adaptive inhibitory capacities with specific regard to the expression of anger and hostile action. That is, losing control of angry or hostile impulses could have extremely punitive consequences, if not death itself. Survival may, to this extent, depend on successful inhibitory capacity, but perhaps at the expense of a "disinhibited" blood pressure.

We also propose that multiple inhibitory demand capacity can be strengthened or weakened by changing nutritional status. The function of CNS and ANS neurons are known to be affected by the cations, individually and in complex interactions. Our investigations will continue to explore the nature of interacting environmental and nutritional influences on blood pressure.

Summary and Future Directions

We have presented here some preliminary evidence that stress and nutrition can interact in interesting ways. So far, we have found suggestive evidence that reactivity to stress is more likely to be attenuated by calcium than potentiated by sodium. Admittedly, we have considerably more data to collect to increase our confidence in these preliminary results.

While we continue to pursue challenging questions about the interaction of stress and nutrition, we are also continuing our efforts to standardize and validate our reactivity test cross-culturally

through collaboration with investigators in the West Indies (Dr. Gerald Grell) and Iceland (Dr. Erikur Arnarson), where interesting parallels and contrasts in the epidemiology of heart disease can be found. Hopefully, conclusive data addressing the important connections between stress, nutrition, and heart disease can be presented to a future workshop here at Meharry.

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Table 1
Frequency of premature ventricular contractions (PVC's) during cardiovascular reactivity testing of a patient with recent coronary bypass.

Test Segment	Length	PVC's	Rate/Min
Baseline	5 min.	21	4.2
Instructions	5 min.	82	16.4
Stress (1)	3 min.	82	27.3
Rest (1)	8 min.*	48	6.0
Stress (2)	3 min.	52	17.3
Rest (2)	2 min.	2	1.0
Stress (3)	3 min.	7	2.3
Recovery	5 min.	1	0.2

*Usually a two-minute segment, but lengthened because of this patient's excessive reaction to the test.

Table 2
Characteristics of Main Comparison Groups (Mn = Mean, se = standard error of the mean, P = Statistical probability of chance outcome determined by t-tests) *(Weight/Height^2) X100

		AGE (yrs)	Height (in)	Weight (lbs)	Body Mass*
Low Na	Mn=	24.2	70.4	185.4	3.72
(N=9)	se=	1.03	0.91	13.26	0.13
High Na	Mn=	22.9	72.1	188.1	3.61
(N=9)	se=	0.99	0.53	5.68	0.07
	P =	.39	.14	.86	.67
PH-	Mn=	23.2	71.3	179.7	3.50
(N=9)	se=	1.05	0.77	11.22	0.16
PH+	Mn=	23.9	71.2	193.9	3.83
(N=9)	se=	1.00	0.82	8.44	0.16
	P =	.67	.89	.35	.19

Table 3
Mean 24-hour Urinary Chemistries for Main Comparison Groups (24-hour period ending 8:00 a.m. of dietary day five).

		Na*	K*	Ca**	Mg**	Na/K	Ca/Mg
Low Na	Mn =	32.8	34.4	77.6	95.5	1.08	0.75
(N=8)	se =	6.77	6.69	23.7	24.9	0.23	0.13
High Na	Mn =	176.6	73.1	92.0	101.2	2.78	0.91
(N=8)	se =	35.1	19.1	22.1	19.9	0.28	0.12
	P =	.001	.075	.68	.84	.001	.42
PH+	Mn =	106.1	63.9	98.3	104.9***	1.73	0.83***
(N=9)	se =	37.0	18.6	27.6	28.8	0.38	0.08
PH-	Mn =	94.1	40.0	68.6	91.9	2.05	0.83
(N=8)	se =	30.2	6.21	10.5	10.2	0.38	0.15
	P =	.80	.29	.38	.70	.59	.94

*mEq
**mg
***N = 8

Mn = Mean
se = standard error of the mean
P = Statistical probability of chance outcome determined by t-tests

Table 4
Correlation Coefficients and Probability Levels from Analyses of Systolic Reactivity and Urinary Chemistries Immediately Preceding Testing.

Delta-SBP and:	r	P
Na	-.03	.85
K	-.14	.60
Ca	-.49	.05
Mg	-.32	.24
Na/K	-.09	.74
Ca/Mg	+.11	.70

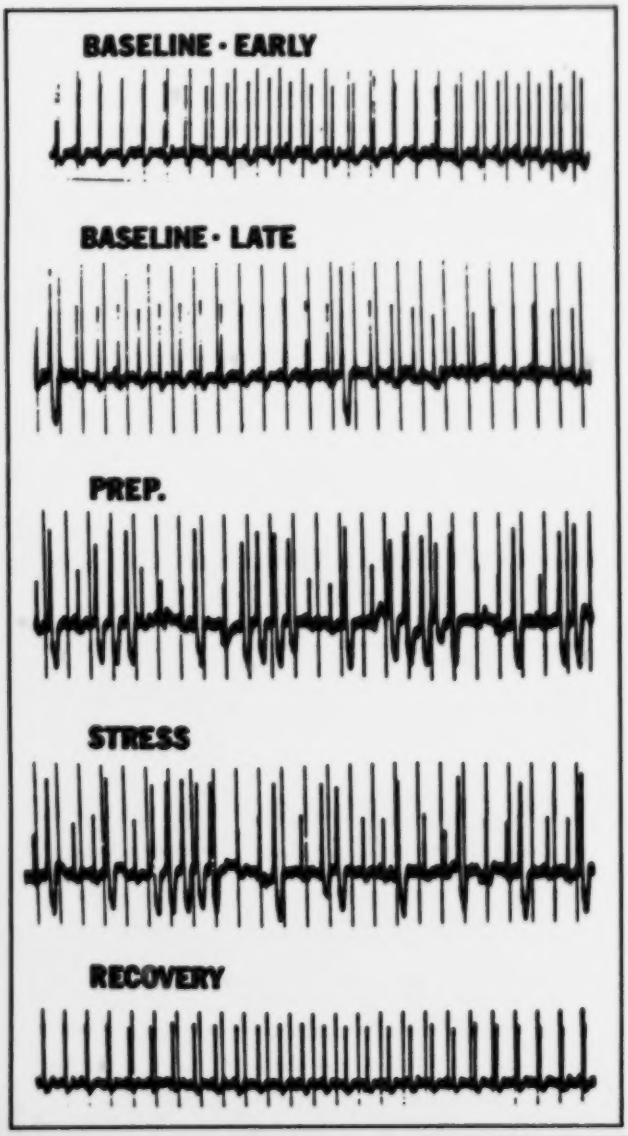

Figure 1. Electrocardiographic records of PVC activity elicited during selected segments of a cardiovascular reactivity test in a patient with recent coronary bypass (PREP: 30-second period immediately prior to the beginning of the first 3-minute segment of stress).

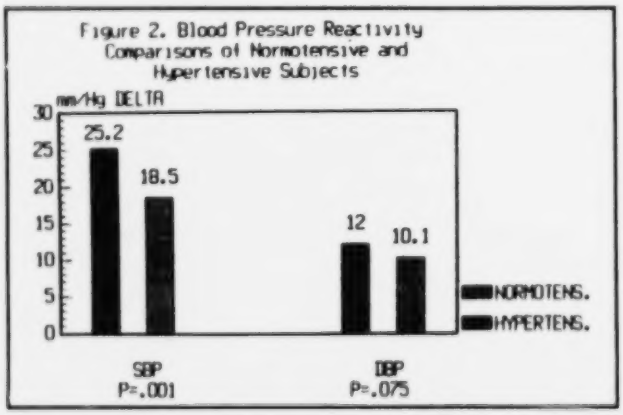

Figure 2. Blood pressure reactivity comparisons of normotensive and hypertensive subjects.

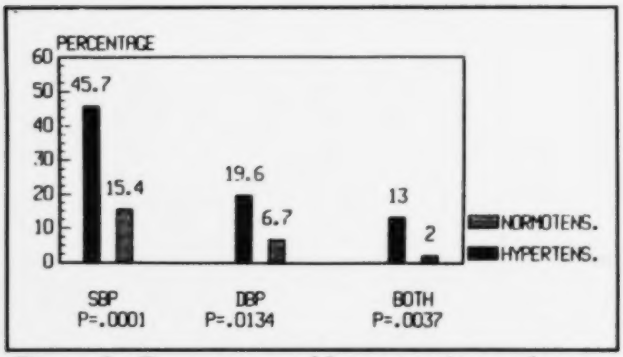

Figure 3. Percentages of hypertensive and normotensive subjects >= 30 mmHg SBP-delta, >= 20 mmHg DBP-delta, and both reactivity criteria simultaneously.

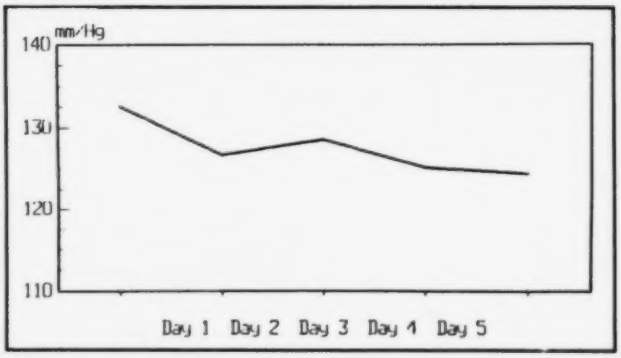

Figure 4. Systolic blood pressures of all subjects combined across the five-day dietary period (pre-breakfast).

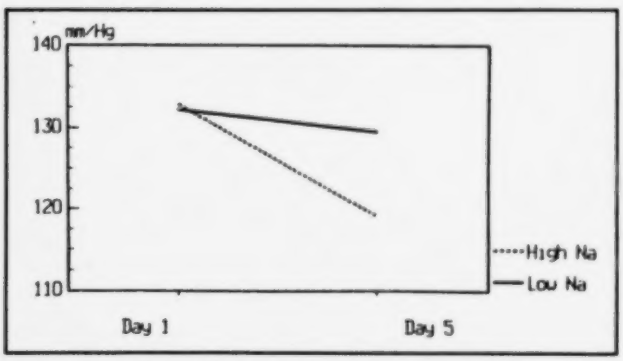

Figure 5. Systolic blood pressures of high and low sodium subjects on the first and last days of the dietary period.

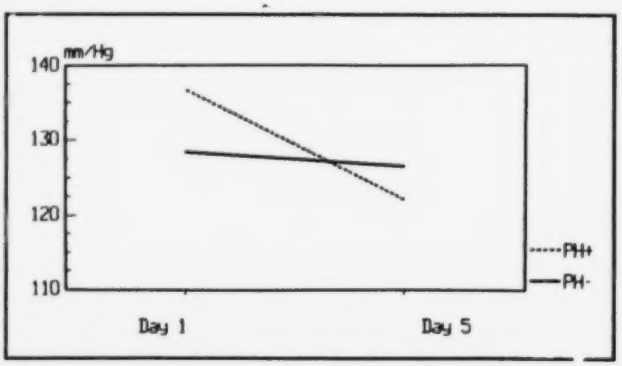

Figure 6. Systolic blood pressures of subjects with positive (PH+) and negative (PH-) histories of hypertension on the first and last days of the dietary period.

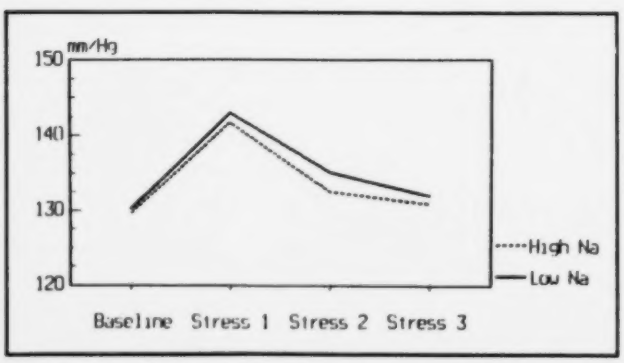

Figure 7. Systolic blood pressures of high and low sodium subjects during baseline and three segments of cardiovascular reactivity testing.

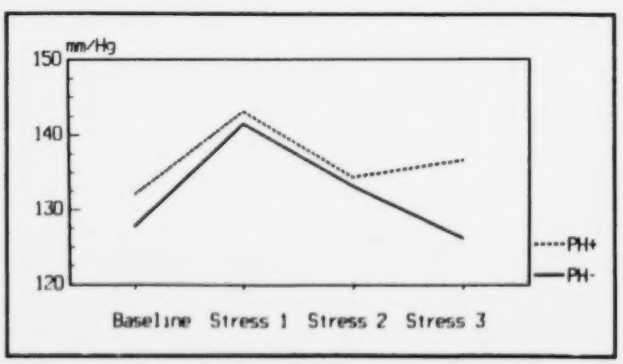

Figure 8. Systolic blood pressures of subjects with positive (PH+) and negative (PH-) histories of hypertension during cardiovascular reactivity testing.

Second Scientific Session: Discussion

Dr. Smith:
I want to ask Dr. Ernst if the excretion of calcium in the urine was higher in those receiving high sodium diets.

Dr. Ernst:
No, it was not. I am glad you asked that. I did a quick, simple T-test comparison of the high sodium and low sodium, and saw no evidence for that.

Anonymous:
(Question inaudible)
Dr. Ernst:
Sure, let me start from the beginning. I thought of that very thing, that perhaps this was an artifact of the sodium sensitivity, or the sodium conditioning, that didn't show up in reactivity testing, but when you compare the amount of calcium excreted by the high and low sodium subjects, there is no significant difference. Moreover, when you compare the amounts of sodium excreted by the parental history positive and parental history negative individuals, there is no significant difference.

Anonymous:
(Question inaudible)

Dr. Ernst:
May be another speaker here can address that better than I can because I am really much more versed in the behavioral aspect of stress testing than I am in the nutritional part. I have not been able to find anyone who has looked at the calcium factor as it relates to cardiovascular reactivity. Almost everything that has been done relates to sodium and potassium. Would you agree with that, Dr. Grim?

Dr. Grim:
Right.

Dr. Thomas:
Dr. Ernst, I was particularly concerned about the baseline level of blood pressure of the subjects that you looked at. It looked like all of them were above 120 and up to 130, and we would classify those as precursors of hypertension in the medical students that we studied. Do you think those baseline tracings are correct, because we found very few that were 130?

Dr. Ernst:
Okay, yes but you were probably looking at those first day blood pressures. Now if you looked at the one slide that showed the adaptation across the five days, on the fifth day you probably saw a more accurate resting blood pressure in these individuals, notwithstanding the fact that half of them were getting high sodium, and I think they were a little bit less than that.

However, if I can address another part that, I found particularly interesting, and I must admit I approached this rather unusually, atleast from the standpoint of these nutritional parameters. When we started, a couple of people had systolic blood pressures over 140. Fortunately, one of them was in the low sodium group, which made me feel a little bit better. Another individual was in the high sodium group. I reported every blood pressure to our physician supervisor as we went along in the study, and interestingly, the high sodium group had an enormous adaptation of blood pressure, which decreased from the 140's down to the 120's.

Dr. Thomas:
I missed the amount of sodium - how much?

Dr. Ernst:
It was 300 milliequivalent, and the low sodium group was 10 milliequivalent.

Dr. Zemel:
Did you look at peripheral vascular resistance or the catecholamine?

Dr. Ernst:
No, and that would be very interesting to do.

Dr. Grim:
I might just comment and congratulate you on a very nice study. We studied 120 sets of twins in Indiana, all white, and showed that those responses were strongly genetic. Not only was the level of pressure genetic, but the movement around that point appeared to be . One of the problems always with family history, we have found in studying college students, that if the student says, "Yes, my parents have hypertension," he or she is usually right. If he says "no, then about half the time the parents may have high blood pressure and didn't tell the student about it. So, one question I have of you is, did you actually measure the blood pressures of the parents?

Dr. Thomas:
We did compressor tests on students and followed them for 25 years ~~to see~~ if we could predict hypertension. It did not correlate well with the incidence of hypertension.

Dr. Grim:
It is the same thing. I think - at least my interpretation of the compressor literature is that it has a very variable track record in terms of predicting certain aspects of the sort. We did not and we do plan to do more extensive follow-up of the actual medical histories of our subjects. There is very recent study - and the author, I am sorry, I can't give you the name, but may be I can get it for you before you leave - which shows very high correlations between subjects' reports of parental history of hypertension and the actual confirmation of that from a medical standpoint. I was very encouraged by that because it meant, for me, at least initially, a lot less work.

Dr. Iacono:
I was interested in your data when you showed the excretion rates of certain minerals, and it was surprising that you got the correlation with calcium in spite of the fact that you were feeding a high level and low level of sodium. I think this is very important. We are now doing this sort of feeding studies, and we are finding some very fascinating data as to the excretion of various minerals when we control the mineral intake levels.
My question is this: Do you have any idea of what the level of mineral intake was in these subjects? Since you were looking at excretion of these minerals, was there any knowledge of what they were eating?

Dr. Ernst:
Yes, by all means. We had all of them - in fact, all of the minerals were quantified. I might mention that I personally supervised the eating of all these meals, which was a very laborious task and I know the amount of food that was not taken in was virtually negligible.

Dr. Thomas:
Talking about your salt factor, it has been noted that certain individuals will develop cardiac enlargement prior to the development of hypertension. I wonder if salt is the only thing that causes a black person to become hypertensive?

Dr. Grim:
Well, certainly not every black person who eats salt or decreases salt changes his blood pressure very much, as Dr. Ernst has shown, and very nicely. It happens in those people who are salt sensitive, whether they are white or black. I think it is some sort of an intrarenal problem, in which there is an increased avidity to retain sodium. We don't know whether that is in the tubule, it could be in the outer stromal system, it could be renin, although the renin tends to be very low, so it is probably not rein.
The LVH (left ventricular hypertrophy) problem is interesting. Left ventricular mass is probably an integrated way to measure blood pressure. In our studies, and I think Dr. Alpert will report on Friday that if you look a 24-hour blood pressure in

black subjects, in L.A., we don't see any decline at night, hardly, in our normal black individuals. That has now been documented in a study in Chicago, and I think Dr. Alpert will tell us the same thing in children. In black children compared to white children there is not as much of a decline in blood pressure at night, or as much of a rise during the day. I think 24-hour blood pressure is going to be very fascinating to look at.

Dr. Enwonwu:

There was a recent report in the British Medical Journal, I believe a few months ago, which looked at several thousand adults in Scotland. They found no correlation between sodium intake and systolic blood pressure, but a very strong correlation between blood pressure and alcohol intake. It worries me, when you get one set of results in one country and something almost contradictory elsewhere. Brenda, you were telling us this afternoon that among native Americans there is a high intake of alcohol as well as a high prevalence of obesity. The blood pressure is low. What could account for these demographic differences?

Ms. Broussard:

Sixty million dollar question, there.

Dr. Grim:

Well, certainly part of the difference could be, particularly in American Indians, that you have got 500 different groups that have really been isolated, many of them for a long period of time, with striking differences, for example, in diabetes. I think there may well be different genetic pools. I think it is going to be very interesting to look at those isolated groups to see if there is any difference. They may give us a clue. If we can figure out why the Pimas, virtually every one get diabetes, we may have some clue to diabetes in general. We may have the same thing if we find those groups that get hypertension or have the greater prevalence of hypertension. The thrifty gene hypothesis for diabetes is biscally a survival of the fittest; that is, those people who survived periods of starvation did so because they stored fat better, and now, in a situation of excess calories, they get fat because they are very good fat storers. I think that is the thrifty gene, and I am sort of suggesting the same thing - thrifty gene for sodium retention. In fact, you could say that every gene that is currently with us has to be thrifty or it wouldn't be here.

Dr. Iacono:

I wanted to ask Ms. Broussard: I know it is very difficult to sort out the degree of state of nutrition with respect to hypertension. You gave two very nice slides, one showing the incidence of hypertension among various categories of Indians, and then you gave a very nice slide showing the overweight problem. I wonder if you correlated these. I thought those were clear data which might show to what degree the incidence of hypertension might be due to overweight in those various groups of Indians.

Now, I know that you showed the bottle of Thunderbird wine, and alcohol certainly is a factor in hypertension. I would gather from your data, at least that which you showed, that you don't have clear information on the intake of alcohol among the Indians. Is that correct?

Ms. Broussard:

That is true. We did take a look at prevalence, selective studies that have been done on prevalence. No, we didn't, say, take Cherokees of a certain year and take a look at the other studies that have been done on nutrition. The problem is, there are so few studies in either category. I don't know of one prevalence study that has been done in the same group, I guess with the exception of Pimas, that also has information on the caloric intake. This is ripe for researchers.

The next one, about alcohol, that is a good question. We know, overall, alcohol is a real public health problem. You start getting beyond that big statement, how much alcohol, how much do you drink, the nature of it - binging versus steady intake! Interesting questions for public health researchers, very political issues in Indian communities.

Dr. Iacono:

In that regard, have there been any studies where you define the entire diet of blacks in various areas of the United States, and/or Indian minorities? By that, I mean where we actually make,

say, a 24-hour recall or a three-day diary and look at all nutrients. For example, what struck me that, on the one hand you showed the very contrasting diet, that is, of the Indian eating buffalo, followed by a lady who was cooking a bread with a high fat content. So, the question then is, what are the diets that these people eat. Are these generally known? Ms. Broussard:

No, it is not known. That is one of the big problems. We don't have good diet data. In the next HNANES survey, we are trying to get at least one Navajo community included. That is still not settled. Ms. Broussard:

Probably the most detained survey, done in 1971 by Reed on the Pimas, didn't even ask about alcohol. That can be a significant source of calories.

Dr. Kumanyika:

Sort of along those lines, I was wondering, since we think that there is a genetic susceptibility, if there is any move toward being more precise about that in the Indian studies? For example, if you were to group the data on hypertension prevalence by ethnic origin of the tribes that are in the same group, would it look different from grouping by Indian health services areas? And, I guess, the same for Dr. Ernst's study - I mean, is black race good enough with the kind of numbers you can mange in this study? Should you be trying to find markers for these sensitivities so that we don't keep getting so much noise in it and saying that we don't know. It is kind of a comment, but it is also a question as to whether or not anything is going on in these areas.

Ms. Broussard:

Just to make a comment on that. If we look at the Nashville area, which serves the east coast, you would have the same data for Seminoles in Florida, which is very different from, say Penobscots in Main. Dr. Ernst:

I honestly can't answer that question. I wonder if Dr. Grim who has more data and more experience than I can relate to that specific question.

Dr. Grim:

No, we certainly don't have. My guess is that a marker for sodium sensitivity would be to give diuretics, and if blood pressure goes down, then they are sensitive, but we certainly don't have any gene markers. Renin levels helps, on the average, but it is not a good enough marker. What we are looking for - there was just an interesting report on the salt sensitive and resistant rat at the hypertension meetings, and the renin gene is different in those two subspecies of rat, so we are going to be looking at the renin gene itself in salt sensitive and salt resistant people to see if it is correlated. It segregates very nicely, as you would expect, in the rat model. Molecular genetics is going to give us a lot more markers to look at and hopefully we will be able to find something. One of the problems, I suppose, in the molecular genetics, I think - I use sickle cell as a classic example-we have known for forty years exactly where the amino acid defect is in sickle cell, and it hasn't helped us one bit yet in figuring out how to best manage those patients. So I wouldn't get terribly excited that we are going to find new methods of treating things based on molecular genetics. We may be able to understand the transmission and susceptibility to the disease better.

Dr. Ahmed:

Dr. Ernst, I would like to congratulate you first on the fine work that you have done. I have a question for you. You exposed these subjects to different sodium intakes for about five days. I would like for you to tell us more about what you think of the duration of this exposure - if the duration is long enough?

Dr. Ernst:

Yes, you know, it is very difficult to factor out the learning component from whatever other factors may be influencing that reactivity. Let me go back to the first part of your question. I am not absolutely certain. It was really on the basis of an outside consultant's opinion that five days were sufficient for the kinds of data that we wanted to look at. I wasn't absolutely convinced that we would necessarily see something happen in the resting blood pressures across the five day period, but I thought for sure it would be an adequate amount of time to test what was really our main hypothesis, and that was the issue of reactivity after five days of the sodium load.

Now, let me just say, I don't know if any of you

have actually implemented a study like this, but those people who report 14 and 21 days of doing studies like this - I don't know how they do it. I'll tell you that we gave these guys $100 apiece to come in for 15 meals and have their blood pressure taken and do two 24-hour urine collections, and I think they made minimum wage. I felt, if we had gone another day longer, I would have lost my subjects. It was just a very difficult thing to implement. So, if we went beyond that five-day period, I think we would need either big bucks or some kind of evangelical motivation to get them to continue.

Dr. Ahmed:

What would be your guess, if you prolonged this period?

Dr. Ernst:

I don't have, at this point, a log of respect for the sodium connection with blood pressure in normotensive individuals, and I think that is an important qualifier. I am not really sure. I think maybe sodium is over-billed when people look at sodium in an isolated way, distinct from the interactive influence of other nutrients. Indeed, throwing in environmental factors make it an even much more complicated picture. Again, this is not a nutritionist giving his opinion - take that for what it is worth-but I would be surprised if we ever find one single factor that is going to exert that kind of influence on the development of a very complex problem, as I think Dr. Guyton made the point very well this morning.

Dr. Grim:

In studies we have done in normals, lowering or rising salt intake, we have found considerable heterogeneity. Some people will go down when you lower sodium intake, some people won't change, some people will go up. Dr. Ernst you showed the average trend was down for both high and low salt. Did you have anybody who went down more - you must have had some people go down more than the average or some people who didn't change or some people who in fact went up?

Dr. Ernst:

That is really a very interesting question. It was only very recently that I did the individual graphs on all eighteen subjects, and the only ones who showed a flat curve were the ones with the lowest systolic blood pressure. I think statisticians, and Dr. Enwonwu would probably agree, that you have what is basically a regression to the mean in all of these subjects, but clearly, there was no evidence in any of the eighteen subjects of any increasing trend across the five day period - none of them. Again, I think it is important to emphasize here, we had eighteen black subjects who were presumably sodium sensitive, more sodium sensitive than whites at least, and nine of those individuals were parental history positive. One would certainly expect to see at least one individuals, especially the one with the 145 systolic beginning pressure, to show some reactivity, and in as much as he did not and others did not, it made me question, at least to some degree, the power of this sodium effect in the normotensive individuals, and I think that is a very important qualifier.

Dr. Grim:

One other comment. It emphasizes the importance of taking multiple measurements before you make a decision on something, because you were under very much the same conditions for five days and saw blood pressures sort of progressively decrease. Your 24-hour urine you reported were 32 and 120 millimole, or 132 millimole, I think. I thought you said you used 300 millimole to load with. Dr. Ernst:

I think it was one hundred and seventy in some, and 32 in the low. That is a good question. I don't know where the rest of that 300 milliequivalent was going, but it certainly wasn't being spilled in the urine. There was probably a small margin of that that wasn't taken in.

Dr. Grim:

Did they gain weight? Did the high salt people gain weight?

Dr. Ernst:

The diet was designed for the average, 175-pound black male. Unfortunately, after the fact, of course, we found out that we had a 185-pound group of individuals. They lost an average of 2.3

pounds, and there were no difference in weight loss between the two groups. How much of that was what, I don't know.

Dr. Enwonwu:

I have a few questions for Dr. Grim. I am interested in the exception rather than the rule. You showed some slides which seemed to suggest that in South Africa the blood pressure was generally higher in whites than in blacks. This seems to be contrary to the trend in other places. Would you care to comment or speculate on the reasons why that should be the case? Are these residents of the city? Do they live in rural areas of South Africa, or what?

Dr. Grim:

I think these were both urban samples, I believe. I would have to look at that again. I am not sure that - on the graph, it looked like it was lower in blacks than whites - it may not be significantly lower, I think, but it certainly wasn't higher. I think that is an interesting difference. We know very little about salt intake in either of those groups. I don't know the history of South African whites. I think it was a fairly isolated group, originally, who migrated down there and settled in that area. Perhaps they came from a higher blood pressure group, I don't know.

The problem with sodium intake, I think, in day-to-day studies - you mentioned the Scottish or Irish study - is that those people who are salt sensitive, if they ate over 80 millimole a day, they have already gotten most of the blood pressure effect, and all of our diets, virtually, are over that. So you are above the sort of threshold effect and you begin to see the separation out, and we have seen it when you go down to 10 millimole a day, or even 50 millimole a day. Then you begin to see some people who do change their blood pressure. But everybody is so much higher, and that is almost worldwide. Those people who are salt sensitive are already above the threshold for sodium intake. In our massive sodium loading studies, when we went to 1500 millimole, we had a couple who had virtually no change in blood pressure. And this was amazing. There were others who went up quite strikingly. There is quite a person-to-person variation in the ability to handle salt. I think there is no doubt about that.

Dr. Edozien:

If I might comment briefly on that question. I think that when you are dealing with third world countries and comparing groups, it is very difficult to make any statements about blood pressure without taking into consideration the differences in body fat. You must correct for body fat before you can make comparisons in third world countries.

Dr. Grim:

Most of these studies that I have gleaned from the literature don't have any weight data, certainly don't have any subscapular skinfold thickness, so we can't adjust for that. But if you look at some of the African studies, for example, you are comparing the bushman, who are the pygmy group, whose average height is about 3 1/2 feet, versus the Watusi, whose average height is 7 feet. Those obviously are quite different people, and you might expect them to have quite different blood pressures, and there is no reason to pool all of those people together, actually. So, even within Africa itself there are striking variations in blood pressure, and whether that is due to difference in diet or geography or genes, we don't know.

Anonymous:

My question is for Dr. Ernst. How did you control/monitor the diet of your subjects when they got to their homes?

Dr. Ernst:

That is a very good question. There was no way that you could control what they did when they got home. The best I could do was to give them a Monday morning sermon. We gave them snacks to take home, including the liquids we wanted them to drink, so that we could keep that marked as well. We thought we covered the 24-hour periods, but there was no way you could know for sure. I was sure there was some degree of individual variation in compliance. On the other hand, our urine chemistries, again, I think, confirmed a fairly strong compliance with what we had them eating. My Monday morning sermon

also included a plea for no recreational chemicals during the week, and I think that was fairly effective.

Dr. Enwonwu:

I raised one question this morning. I don't believe it was answered, and I am sorry to raise it again. There are some studies showing that if you load animals, with another sort of sodium, let us say sodium acetate or sodium citrate, instead of sodium chloride, many of the effects that are attributed to sodium disappear. The question has been raised, are these blood pressure changes really due to sodium, or are they due to chloride. Do you have any information?

Dr. Grim:

Well, not only in animals, but in man. There is a nice study published in the New England Journal where they took salt sensitive people, men and fed them either sodium chloride, in a randomized design, and then sodium citrate. When they gave sodium citrate, same amount, same millimole, there was no rise in blood pressure, no rise in plasma volume, no fall in hematocrit, compared to when they gave sodium chloride. So the question is that you have to have at least sodium and chloride. It is tough to give chloride alone. You have to give ammonium chloride, which changes the pH. It is very tough to give chloride along to man, anyway; you can do it to animals. We have done some similar studies. We have looked at sodium excretion in sheep now, feeding sodium chloride and sodium citrate, and a sheep will dump sodium citrate much faster when he eats it than he does sodium chloride, suggesting that the two ions are handled together quite differently than separately.

Dr. Thomas:

I think the work of Dr. Lewis Jones points out very well, that sodium citrate doesn't affect the blood pressure and sodium chloride does. Dr. Ernst:

I want to mention in addition to that, just for the record, that our subjects got five grams, one germ per day, of sodium chloride. The rest was presumably in the food in the form of sodium. I say that because many studies, so-called high sodium studies, increased the sodium by a lot of sodium chloride per day.

Dr. Enwonwu:

Is there any evidence for chloride as opposed to citrate increasing the renal conservation of sodium?

Dr. Grim:

In the studies I did in man, there were no weight changes. In our sheep studies, when we fed sodium citrate, in fact, we got a negative sodium balance. In other words, when we fed sodium citrate, we got more sodium in the urine than we are giving. The
first time we did that, I thought my fellow had weighed the stuff out wrong or calculated wrong. It suggested that when you don't have the chloride, you are liberating sodium from someplace else, may be the bone. Some other stores of sodium are being mobilized without the chloride. So I think that should be a very active area to look at - what exactly is going on?

Third Scientific Session

Chair **Eugene Grossman, M.D.**

SODIUM AND POTASSIUM STATUS IN HYPERTENSION

Elijah Saunders
Hypertension Division
The University of Maryland Hospital
Baltimore, MD

Dietary Sodium and Hypertension

Numerous studies have been reported over the years implicating sodium as a factor in the pathogenesis of hypertension. Most of these data were based upon epidemiological studies which showed that unacculturated populations with low levels of salt intake did not have much hypertension. Such populations included the Yanomamo Indians (1), Carazos Amazonians (2), Pukapukans (3), New Guinea Highlanders (4,5), and American Eskimos (6). In addition, there have been reports of many communities in the world which seem to have low blood pressures or, at least, the blood pressure does not rise with age, and these include a number of communities in Africa, namely, in western Kenya, northern Kenya, eastern Uganda, Ethiopia, Botswana and Tanzania (7). Similar communities exist in other parts of the world, for instance, in the Far East: Oceania, China, Australia, and in Asian countries such as India, Malaysia, and parts of Brazil in South America (8). It has been speculated that the most likely reason for these low blood pressure communities is a diet which is lacking in salt. However, one cannot rule out the role of physical activity, the absence of stress, or the presence of bacterial and parasitic infections in many of these areas. However, it is very clear that in many of these communities, one of the most common factors is a very low sodium chloride intake in the diet. One certainly has to be careful in extrapolating epidemiological data to indicate causative factors in disease.

Animal Data Implicating the Role of Sodium and Hypertension

The description of two strains of rats by Dahl (9,10), in which one strain is salt sensitive (S) and one salt resistant (R) gave some insight into the role that sodium may play in hypertension. Studies on these populations of rats indicate that genetics play a role in causing the "sensitive strain" of these rats to elevate their blood pressure with very small amounts of sodium in the diet, as compared to those which were classified as salt "resistant." This has some parallelism with certain human populations which seem to be more sensitive to the ingestion of sodium in terms of elevating the blood pressure than other populations (11). Studies by Luft and others (12,13) suggest that this phenomenon is more common in black hypertensives.

Dietary Sodium in Blacks and Whites

As indicated above, a variety of the studies from various places around the world have suggested association with dietary sodium and hypertension. Probably one of the first studies done to demonstrate the role that sodium may play in the treatment of hypertension was that of Dr. Kempner's (14,15), in which he placed subjects on a diet fairly low in sodium (below 150 mg. per day) and relatively high in potassium (about 3000 mg. per day) and in which the food contained only rice and fruit. He was able to produce a lowering of the blood pressure. These studies led to speculation that, possibly, populations with high

hypertension prevalence (i.e., black populations) may consume more salt than comparable non-black populations. Numerous studies have been done and summarized in Table 1, looking at the sodium intake of hypertensive blacks and whites. In these studies, neither the dietary nor the 24-hour urinary collections showed any evidence for higher sodium intake in black men or women despite a higher average blood pressure and an almost three-fold higher prevalence of hypertension. Other studies which have been done (17-20) have failed to show a higher sodium intake in blacks. The 1976-82 National Health and Nutrition Examination Survey (21) indicated that, although there was no racial breakdown, there were no appreciable differences in the sodium intake of Americans above and below the poverty level. Thus, to summarize this data, it would seem that there is no proof, in spite of some of my empiric observations, that blacks consume any more sodium than whites in this country. The difference, however, does seem to be in salt sensitivity because of the probable genetic predisposition toward a reduced excretion rate of sodium by the kidneys of many blacks compared to whites.

Interaction Between Dietary Sodium, Potassium, and other Ions

Whereas there has been no demonstration that blacks consume any more sodium in the diet than matched white groups, this does not seem to be true for potassium. Table 1, in addition to dietary sodium, also cites ample evidence for lower dietary potassium in blacks. Twenty-four hour urinary excretions of potassium in these studies range from 24 to 45 mEq. in blacks and from 36 to 73 mEq. in whites. This amounts to a 32-38 percent lower dietary potassium intake found in blacks in general and particularly in the hypertensive population. Studies done in Louisiana by Berenson (22) have shown a lower potassium intake in blacks compared to white children. Dr. Langford, whom we have been privileged to have just heard, has also shown in 24-hour blood pressures and electrolyte excretion over a period of six days, a strong correlation between the sodium-potassium ratio and diastolic blood pressure. Thus, with the demonstration of the lower potassium intake, the higher sodium-potassium ratio found in the urine of blacks was more strongly correlated with an elevated blood pressure than the excretion of sodium per se (23). Additional studies by Langford and Kushman of 407 black and 216 white males with untreated hypertension, which encompassed five Veterans Administration hospitals in the eastern United States, indicated that black males excreted only 62 percent as much potassium as white males (23). Thus, it seems that dietary potassium may be at least as important as dietary sodium intake in the regulation of blood pressure in blacks. Studies have also correlated stroke mortality with the sodium-potassium ratio, and a positive correlation has been shown (24,25).

Recent data are emerging implicating the role magnesium plays in terms of its interaction with sodium and in causing hypertension. Dr. Langford in the previous presentation emphasized the inverse relationship between dietary magnesium and high blood pressure, and this no doubt plays a very important role in the high rate of hypertension in blacks. I suspect that the relationship is very similar to the one between sodium and potassium in causing hypertension. More data need to be collected in this area.

The role that calcium may play in hypertension has received much attention over the past few years, being popularized by McCarron (26-29). All of these studies indicated a lower dietary calcium intake in hypertensives when matched with normotensives for age, race and sex. This correlation seemed to be most marked in many American blacks compared to white groups, and it seemed to play a role when the minimal recommended dietary calcium intake of 800 mg. per day is not met. One would have to speculate as to the reason that blacks may be more deficient in dietary calcium and also potassium, as mentioned. Many investigators suspect that the reasons for this discrepancy is related to socio-economic factors. The suggestion is that blacks do not eat as much potassium rich foods (fruits and vegetables). Such foods are probably less accessible and cost more, whereas fast food, canned and processed foods are more accessible but contain more sodium and less potassium.

I also suspect that a cultural or ethnic habit plays a role in a reduced preference for potassium-rich

foods on the part of many blacks. As far as calcium is concerned, again one might speculate that dairy products, which are high in calcium, may not be as accessible and as affordable as non-dairy products to many blacks or otherwise economically deprived groups. The issue of the high rate of lactase deficiency in blacks leading to less consumption of milk and similar foods could also be responsible for the low dietary calcium. Studies have been reported by Sowers, Laragh, and others suggesting that sodium sensitivity is greatest when there is a lower level of serum ionized calcium, reflecting a lower dietary calcium intake. Even though I think that there is a subset of hypertensives in which the lack of calcium may play a role, I believe the data are far too scanty at this point to suggest that a large number of hypertensives fall into this group. Specifically, I do not think the data are sufficient to suggest that the lack of dietary calcium is a major cause of hypertension in blacks. A limited number of patients have been reported by Resnick to have responded to supplemental calcium with lowering of their blood pressures.

Therapeutic Implications of Sodium and Potassium Status and Hypertension

The average American consumes approximately 10-20 grams of sodium chloride each day on a typical diet (30). Approximately two-third of this comes from the natural sodium content of foods or processing, and one-third is added from a salt shaker while cooking or at the table (31). Although the Kempner diet, which was very low in sodium, resulted in a drop in blood pressure, this degree of salt restriction is not felt to be practical for the average individual. However, moderate dietary restriction of salt to about one-half the amount normally consumed by the average American has been shown to result in an approximate 10/5 mmHg drop in blood pressure (32). Studies by other investigators have confirmed the modest drop in blood pressure with the restriction of sodium alone. Thus, it would seem that for mild hypertension, patients should be given a trial of a moderate restriction of sodium in the diet in an attempt to control the blood pressure. However, according to the World Health Organization, if the diastolic blood pressure is not below 90 mmHg after three months, such a non-drug regimen should be abandoned (33). Many patients have told me that they would prefer eating salt and taking extra amounts of diuretics in order to control their blood pressure. Most clinicians believe that even with diuretic therapy, one can better prevent hypokalemia if there is also a moderate restriction of sodium in the diet. Again, this is a problem for most Americans and not any more prevalent in the black community. The exception, however, to this rule has to do with many of the ethnic menus ("soul diets"), which are heavily seasoned with salt and other condiments, as well as having high fat content. I have suggested to the black community that effort should be made to "soulize" their food without "sodiumizing" it. Food manufacturers are now experimenting with ethnic diets which will have the taste but not the harmful effect of many of these menus (i.e., sodium, fat, cholesterol). I counsel my patients on the sodium content of many commonly eaten foods. These are shown in Table 2 (34). This table shows the surprisingly high sodium content of such common foods as processed cheese, 2 percent cottage cheese, white bread, many seafoods, and soups. Many of these foods, especially hot dogs, lunch meats, and fast foods, are consumed heavily in the black community. Therefore, this must be emphasized to both physicians and patients.

When one talks about the role that salt in the diet plays in hypertension, the issue of the additive effect of excess weight and hypertension comes into play. Numerous studies, including the studies of the American Society of Actuaries, report that obesity was the single condition most often associated with hypertension (35). The Evans County Study (36) showed that residents who gained 10 pounds or more over a six year period developed hypertension twice as often as those who did not gain weight. Other studies have been done in which antihypertensive medications were withdrawn from obese and nonobese individuals, and there was a greater relapse in the hypertension in the obese individuals (37). Thus, it seems that a total dietary approach in treating hypertension should include salt restriction, adequate potassium, magnesium and calcium in the diet and weight control. All of these factors seem

to be magnified in the black community, and whatever role they play seems to contribute significantly to cardiovascular morbidity and mortality in this population.

Before concluding, I think it is fair to say that the medical community has been somewhat ambiguous and paradoxical in its advice to the public regarding eating, especially as concerns cardiovascular disease. For instance, it seems that many of the foods that are recommended because of their low fat and low cholesterol contents (i.e., 2 percent fat cottage cheese) may contain large amounts of sodium (i.e., 40 mEq). Similar analogies can be made with foods that are high in calcium (i.e., milk products) and are also high in saturated fat. Certainly, in many low income, low education and disadvantaged communities, this type of ambiguity is difficult to deal with and, therefore, becomes very challenging to the therapist or those who are concerned with prevention of disease, especially in these populations. Proper counseling, understanding ethnic habits, and appreciation of different cultures are extremely important in placing the proper role that diet plays in hypertension and other cardiovascular ailments.

Summary

Early indications that dietary electrolytes such as sodium and potassium play a role in hypertension were primarily epidemiological, observing unculturated societies in which there were low levels of hypertension, even with age, and comparing these societies with culturated societies in which dietary electrolytes such as sodium were plentiful. These clinical observations and associations were correlated with studies done in animal populations which seem to serve as a model for the study of human hypertension. The high incidence and prevalence of hypertension in the black community led to early speculation that the black population consumed more sodium (sodium chloride) than the general population. However, numerous studies have failed to draw this conclusion. It seems, rather, that it is the handling of sodium by the kidney (greater salt sensitivity) by many hypertensive blacks and the interaction of sodium with potassium, probably magnesium and calcium, which offers a better explanation of these observed phenomena. Some genetic basis would seem to explain this phenomena rather than environmental factors such as dietary habits. On the other hand, it does seem that ethnic and cultural habits which are a part of environmental influences contribute heavily to dietary factors, playing a role in hypertension pathogenesis and prevalence in individuals who are "genetically predisposed."

From a therapeutic point of view, although it has been possible to reduce blood pressure, when it is mildly elevated, by moderate sodium restriction, it seems that weight loss and, in some cases, increased dietary consumption of potassium, magnesium and calcium, may be even more efficacious. Drug therapy for hypertension also seems to be influenced by dietary factors in that diuretics appear to work better in salt sensitive hypertensive populations. Although calcium antagonists also work well in this population, the adverse effect of sodium may be blunted by this particular class of drugs. Obviously, many more studies need to be done to define the interaction between dietary factors and drug therapy in hypertensive populations.

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TABLE 1
Dietary sodium and potassium intake in normotensive and hypertensive blacks and whites

Author(s) (Location)	N	HBP, MM HG	HBP, %	URINE NA^+, MEQ/24 HR	URINE K^+, MEQ/24HR	NA/K RATIO
Grim et al., 1980 [167] (Evans County, Ga.)	BM: 36	130/82	20	130	24	5.4
	BF: 53	136/81	23	131	27	4.9
	WM: 105	127/77	8	162	40	4.1
	WF: 121	124/73	8	135	36	3.8
Watson et al., 1980[507] (Jackson, Miss.)	BF: 491	116.0*		112	28	4.1
	WF: 181	109.1*		98	36	2.9
Hall, 1977[172] (Atlanta)	BF: 72	148/101	100	142	34	4.2
	B: 72		0	127	31	4.3
Barlow et al., 1982[35] (Johannesburg)	W: 34		0	167	59	2.9
	B: 77	88+	0	166		
Luft et al., 1982[300] (Indianapolis)	W: 270	85+	0	150		
	B: 94	87+	0	172	44	3.9
Luft et al., 1983[301] (Indianapolis)	W: 94	83+	0	158	65	2.4
	B: 407		100	176	45	4.5
Cushman and Langford, 1983[88] (Jackson, Miss.)	W: 216		100	184	73	2.9

*Systolic blood pressure
+Mean arterial blood pressure
*Reference #16

Table 2
Sodium content of certain foods

Food	Quantity	Sodium (mgs)	Content (mEq)
Whole milk	1 cup	120	5.3
Cheese			
- Processed	1 ounce	406	17.6
- Cottage, 2% fat	1 cup	918	40.0
Bread			
- White enriched	1 slice	117	5.3
- Buns, hot dog, enriched	1 bun	202	8.8
Corn flakes	1 cup	251	11.0
Apple pie, 9"	1/6	482	21.2
Seafood			
- Crabmeat, packed, drained	1 ounce	200	8.8
Lobster	1 pound	1359	61.6
- Shrimp, fresh	1 pound	635	27.9
- Tuna, packed in water	1 cup	1733	76.3
Olive	1 medium	156	6.9
Meat			
- Corned beef	3 ounces	937	41.2
- Chipped beef	3 ounces	3660	161.0
- Bacon	2 ounces	386	17.0
- Bacon, Canadian	2 ounces	1072	47.2
- Ham, cured	2 ounces	427	18.8
- Bologna	2 ounces	737	32.4
Nuts, mixed, salted	1 cup	280	12.3
Butter	1 tablespoon	140	6.2
Barbecue sauce	1 tablespoon	127	5.7
Catsup, tomato	1 tablespoon	156	6.9
Mustard	1 tablespoon	195	8.8
Soup			
- Pork and beans	1 cup	1008	44.0
- Beef noodle	1 cup	1872	82.4
- Chicken noodle	1 cup	979	43.1
Dill pickle	1 large	1428	62.8

CALCIUM, MAGNESIUM AND HYPERTENSION

Herbert G. Langford
Endocrinology and Hypertension Division
The University of Mississippi Medical Center
Jackson, MS

Calcium and magnesium may be of importance in hypertension in the following ways: 1) The intake of these cations could be one of the epidemiological factors which affect the prevalence of hypertension. 2) Change in calcium or magnesium intake could influence blood pressure, either to rise or to fall. 3) The occurrence of hypertension could affect calcium and magnesium homeostasis, 4) or the therapy of hypertension could affect calcium and magnesium homeostasis.

There is some evidence on each of the above topics, usually unsatisfactory and contradictory.

Calcium Intake and the Genesis of Hypertension

Mary Jane Watson, a nutritionist and the wife of my epidemiological colleague, Dr. Robert Watson, noted the low calcium intake as derived from diet histories of rural and low income children in Jackson, Mississippi and surrounding Hinds County. We noted a stairstep relation in the blood pressures of these individuals as one descended from the upper income to the lower income levels, with progressively high pressures as the families' income decreased. The pressures of the rural individuals were even higher. We found the same stairstep relation in the urinary Na/Ca ratio (1). However, our data on the relation between blood pressure and calcium excretion, or Na/Ca ratio in this population was not consistent, and we abandoned our interest in calcium for our interest in potassium.

In the last few years there have been a number of epidemiological articles on the relation between calcium intake and blood pressure. Data from the National Health and Nutritional Examination Survey have been used to show that there is a negative correlation between calcium intake and blood pressure (2), a negative correlation between calcium, potassium and sodium intake and blood pressure (3), and no correlation between calcium and blood pressure (4). A partial explanation for the discrepancies can be found in the report by Reed (5). He analyzed data obtained from 8,000 Japanese men. The basic data were derived from a 24-hour diet recall, but it was validated with a 7-day diet record in 329 participants. He found a significant negative correlation between calcium and blood pressure and a significant and more impressive positive correlation with alcohol. There was a significant correlation between potassium intake and intake of protein, fat and calcium. When potassium intake was regressed against the other nutrients, only potassium remained significantly associated with blood pressure. Dr. Reed concluded that because of multi-collinearity between the intake of a number of nutrients, it was impossible to tell whether any one of the nutrients alone was responsible for the observed differences in blood pressure.

Racial and Socio-economic Effects on Calcium Intake

The calcium intake of blacks at all ages is substantially less than that of whites. However, the socio-economic gradient of calcium intake is much less than the socio-economic gradient of potassium. Therefore, if increased calcium intake protects one from hypertension, the low calcium

intake of blacks could help to explain the greater incidence of hypertension in blacks than in whites. However, the socioeconomic gradient in the incidence of hypertension is much better explained by the gradient of potassium intake. Of course, both factors could be operative.

Physiological Findings Suggesting a Role for Calcium in Blood Pressure

There seems to be a significant positive correlation between urine calcium excretion and blood pressure. There also seems to be a significant positive correlation between parathyroid hormone levels and vitamin D3 with blood pressure. In addition, there seems to be a significant correlation between total calcium in the sera and blood pressure. A reasonable explanation for all these findings, except the elevated serum calcium, is that there is a pressure calciuresis just as there is a pressure natriuresis. The pressure calciuresis lowers serum ionized calcium. However, unlike the case of sodium, homeostatic mechanisms do not bring the calcium excretion back to normal. Instead, it is likely that the body approaches homeostasis by increased gut absorption of calcium.

It was mentioned above that total calcium seems to have a weak positive correlation with blood pressure. It is theoretically possible to have lowered ionized calcium and increased total calcium. As hypertension becomes more pronounced, there is more ultrafiltration of plasma through the capillaries, and therefore, elevated protein. Part of the protein will have bound the calcium. At the same time, ionized calcium, which would not be ultrafiltered, could tend to be lowered due to the urinary loss of calcium.

An additional factor affecting calcium homeostasis is the interaction between the sodium, intravascular volume, and calcium. Sodium loading increases calcium excretion. This is because increased sodium intake increases intravascular volume, which in turn depresses proximal tubular reabsorption. Much of calcium is reabsorbed in the proximal tubule and, therefore, increased intravascular volume depresses proximal tubular reabsorption. Additionally, urinary excretion of calcium is increased.

Thus, it can be argued that increased salt intake would raise blood pressure. Once blood pressure was raised by increased salt intake or by other mechanisms, calcium excretion is increased, due to expanded intravascular volume and pressure calciuresis. The hypertensive animal or man, especially if the hypertension were caused by increased salt intake, would need more calcium. Would the homeostatic mechanisms which increase calcium absorption, such as increased parathyroid hormone and increased vitamin D3, increase or decrease blood pressure, and would the slightly lower ionized serum calcium produced by the increased urinary loss of calcium have an effect on blood pressure?

Acute Effects of Calcium Infusion and Parthyroid Hormone Injection

The acute effect of calcium infusion is to raise blood pressure. This result would be expected from the effect of calcium on a vascular strip in vitro. Increasing calcium concentrations cause increase in contraction. Parathyroid hormone injected acutely lowers the blood pressure. Therefore, it would be expected that calcium loss produced by sodium loading and/or hypertension would tend to lower the blood pressure by reducing the blood level of calcium, and increasing the blood level of parathyroid hormone. It is of some interest that Kurtz and Morris found opposite changes (6). Giving large amounts of calcium to rats developing DCA-salt hypertension lowered blood pressure. In apparent conflict with this finding is the observation that blood pressure of patients with hyperparathyroidism tends to be slightly higher than of control subjects without hyperparathyroidism, and the difference in pressure is not explainable on the basis of renal damage.

Effect of Chronic Calcium Loading on Blood Pressure

Results have been discordant, both in man and in experimental animals. McCarron has reported that increased calcium intake lowers standing systolic blood pressure (7). Singer and MacGregor found no effect from calcium supplementation in a one month study (8). Kaplan found no mean effect, but some patients increased their pressure, and some decreased their pressure, after 2 months of calcium ingestion (9). Very large increases in

calcium intake given to rats on a high sodium diet tend to lower their pressures, but lesser amounts have either no effect, or in a few studies, have been associated with elevated blood pressure (10).

Effect of Antihypertensive Agents on Calcium Homeostasis

Thiazide diuretics produce decreased urinary calcium excretion. This is probably because the volume depletion produced by the diuretics causes increased proximal tubular reabsorption, and therefore, less calcium available for excretion. The final consequence in terms of the body's reaction is the same as a very low sodium diet. Both of these maneuvers (a low sodium diet and thiazide administration) are, therefore, effective ways to put someone into positive calcium balance. The decreased serum alkaline phosphatase in thiazide treated hypertensive patients reported by Curb, et al, could be due to a positive calcium balance, and therefore less bone turn-over (11). In fact, the high amount of calcium reported to be necessary to keep post menopausal women in calcium balance can be considered as a sodium-mediated increased nutritional demand. It is quite probable that individuals on a low sodium intake would need much less calcium to remain in balance.

In summary, it is clear that there are interactions between calcium, blood pressure, and sodium intake. It is not clear that increased calcium intake will warrant blood pressure rise, nor that increased calcium intake will lower established hypertension. It is clear that calcium effect, if it exists, to lower blood pressure is too little for it to be a clinical approach to hypertension. It is also clear that an increased salt intake does produce an increased calcium need, and it is possible that hypertension also produces an increased calcium need.

Magnesium and Blood Pressure

The confused relation between calcium and blood pressure is closer to solution than the relation of magnesium and blood pressure, if only because there is so much more work which has been done on the calcium question. A superficial argument can be made in this vein: Calcium and magnesium can be considered as antagonistic cations, especially for vascular contraction. Calcium channel-blockers lower blood pressure, therefore, magnesium should lower blood pressure. This line of reasoning is of little help, because it will not predict whether magnesium intake is adequate, whether there is any hypertension associated magnesium loss, and whether one can successfully give increased magnesium to patients.

Epidemiological Data

The epidemiological data on magnesium and high blood pressure are scantier than the data on calcium and high blood pressure. The modern diet probably has much less magnesium in it than the diet of primitive man. Myocardial infarction may be less frequent in areas that have hard water than areas that have soft water. The "hardness" of water is primarily a function of the calcium and magnesium content. However, the hard water story is not tied in closely to blood pressure, and also is not universally accepted as a factor in the incidence of myocardial infarction.

Physiological Control of Magnesium

The mechanisms which control magnesium absorption and excretion are not well defined. For instance, parathyroid hormone does not seem to have a major effect on urinary excretion of magnesium. However, aldosterone, at least in pharmacologic amounts, has a major action to increase magnesium excretion (12). It is not clear whether this action is direct, or due to increased intravascular volume depressing proximal tubular reabsorption of magnesium. In contrast to calcium, urinary excretion of magnesium is probably increased in the thiazide treated patient. Therefore, it is likely that the increased aldosterone of thiazide produced sodium depletion is a cause of magnesium wasting.

Magnesium also interacts with potassium (13). Patients who have marked magnesium deficiency waste potassium. The mechanisms of this correlation are not well worked out, but apparently, the magnesium deficient renal tubule fails to reabsorb potassium normally, and therefore, more magnesium is excreted in the urine. The clinical importance of this finding is that magnesium supplementation may be necessary to correct refractory hypokalemia, especially when magnesium deple-

tion has been one of the causes of the hypokalemia.

Effect of Change of Magnesium Intake on Blood Pressure in Man

Intravenous infusion of magnesium salts is a time-honored means to reduce blood pressure, especially in preeclampsia and eclampsia. The amounts of magnesium infused are rather large, and frequently double or triple the serum magnesium levels. The results of oral magnesium supplementation have been less consistent than the results of a high dose of intravenous therapy. A randomized trial of the effect of magnesium supplementation on blood pressure in diuretic treated hypertensive patients showed significant blood pressure lowering effects in the magnesium treated group (14). In a study of patients not receiving other antihypertensive agents there was no effect of magnesium supplementation on blood pressure. As noted above, the thiazide treated patients were probably magnesium depleted.

Animal Studies

Magnesium deficiency in rats has been associated with increased vascular reactivity and elevated blood pressure (15). Moreover, there are now two studies that showed that magnesium supplementation at a reasonably physiological level will produce chronic lowering of blood pressure, or at least block the rise in blood pressure in SHR rats. It is not known whether the magnesium had any deleterious effects, and clearly these studies need to be continued.

Clinical implications

It will be seen that the epidemiology, the response to therapy and the pathophysiology of magnesium handling are all in need of further work. In addition, magnesium supplementation is quite difficult. Many of the magnesium supplements produced diarrhea. Magnesium diglycine has been said to have less tendency to produce gastrointestinal symptoms than other magnesium preparations. Determination of the role of magnesium supplementation in clinical practice will be dependent on the availability of a preparation that can be tolerated.

Summary

Epidemiological studies often show a negative correlation between calcium intake and blood pressure. Increased sodium intake and probably elevated blood pressure produce increased urinary excretion of calcium. The results of calcium supplementation on blood pressure are inconsistent and probably small. Magnesium deficiency may raise blood pressure, and some studies have shown decreased blood pressure after chronic magnesium therapy.

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DIETARY FIBER AND HYPERTENSION

Frank Sacks
Channing Laboratory
Harvard Medical School
Boston, Massachusetts

Manuscript Not Available

Third Scientific Session - Discussion:

Dr. Grossman:

In preparation for my chairmanship of this session, I looked at the topics. Last year, I had spoken on the relationship of sodium, potassium, magnesium and calcium to hypertension and so I thought I knew a little bit about that. When I looked to see what Dr. Sacks was going to talk about, I had to admit that I knew next to nothing. I quickly did a couple of paper research, and I came up with just two interesting statements I will throw at him to cogitate.

One is a little sentence from a paper by Jim Anderson, who many of you may know as sort of "Dr. Fiber" in this country, ever since his association with Quaker Oats. He talks about what the problem is in all of the fiber studies, and he says, "Many other dietary factors also affect blood pressure," and he lists all the other things, so he says, "and some of the longer term studies also restrict energy and salt intake, and thus the independent effects of dietary fiber on blood pressure remain unclear."

There is a very recent paper in the American Journal of Clinical Nutrition by some of the Australian investigators that Dr. Sacks is very familiar with. The lead off here in this article is Barry M. Margitts, and he describes a painstakingly thorough study in which all of the things you and I might think should have been controlled were, in fact controlled, and he comes to three conclusions.

Conclusion number one is, I don't know why vegetarians have lower blood pressure than non-vegetarians. Conclusion number two, I have shown you it is not due to an altered P to S ratio, because when we did that nothing happened. Number three, it is not due to the fiber content of the vegetarian diet, because when we kept everythng else constant and increased the fiber alone, double blind (they did this by incorporating the fiber in some biscuits that both groups had to eat), nothing happened particularly. So we don't think it is the fiber, and we don't think it is the P to S ratio, and we don't know what it is. And I will give Dr. Sacks a chance to say what he thinks it is.

As a courtesy, one of our prior speakers asked if he could have the floor for just a couple of minutes and make some comments on the program this morning. Would you like to come up Dr. Edozien?

Dr. Edozien:

Mr. Chairman, ladies and gentlemen, the comment I want to make is that, in these studies of diets and blood pressure, part of the confusion is that the correct things that affect blood pressure aren't really being measured.

When you alter the diet and blood pressure is affected, we seem to be paying attention mostly to sodium, potassium, and calcium, but those may not be the most important things. The important things are that some of the hormones that affect blood pressure are greatly altered by these dietary factors, and insufficient attention is being paid to these hormones. The most important things that seem to affect blood pressure are blood volume and the sodium-potassium ATPase, calcitonin and parathyroid hormone. If we measure these and look at their relationship to blood pressure, much of the confusion will disappear. For example, if we take the confusion between what happens when sodium is retained and when we give sodium, the reality is that when we give sodium, we expand the plasma volume and that

tends to increase blood pressure. But at the same time, sodium through a feedback mechanism, reduce ACTH and sodium-potassium ATPase, which reduce blood pressure. So the net effect is that it is very difficult to change blood pressure just by giving sodium. Yet if you disturb the mechanism for retention of sodium and excretion of potassium, whether by norepinephrine, ACTH, cortisol, or any other means, you get a tremendous change in blood pressure, because retention of sodium due to alteration of sodium-potassium ATPase means at the same time that angiotensin II is increased and blood volume is increased. This double change then affects blood pressure, whereas you cannot bring it about by simply feeding sodium, and that happens with most of the other nutrients, calcium, potassium, and so on.

Now, a simple experiment which I want to show here is what happens, for example, with alcohol, which has not been mentioned. In this experiment, what we did, simply, was to give intraperitoneal injections of alcohol, glucose, and sucrose, the rationale being that by giving intraperitoneal injections, we could alter the plasma volume, and through altering the plasma volume change the blood pressure and see the response to this. And when we did that, we found that with alcohol, glucose, and sucrose, the hemoglobin went up because of a decrease in plasma volume. It did not happen with a sham, which was just simply giving the needle, water, or saline. And, with glucose, you see that the glucose has gone in because the glucose level has increased, and with that increase in glucose level, comes an increase in insulin which does not occur with other things and alcohol has increased also. Again, because of the fall in plasma volume and the reduction in blood pressure, you see the response. The noradrenaline (NE) is there, and with alcohol, glucose, and sucrose. Once blood pressure goes down because of the dehydration, NE and epinephrine go up. ACTH goes up. So these are the major hormones that affect blood pressure. By lowering blood pressure, you produce a reaction in these hormones, ACTH and corticosterone. So these are responses to dehydration and a fall in blood pressure. But the alcohol and glucose have other specific effects, which I will show you in the last transparency. In addition to the changes due to dehydration, alcohol specifically has the effect of raising calcitonin, and many of the other effects of alcohol on blood pressure can be related to the calcitonin. Glucose, you see, has a specific effect on parathyroid hormone, and this change in parathyroid hormone is part of the mechanism by which carbohydrates produce other effects on blood pressure. So the important thing is that these dietary factors alter a whole lot of hormones, and it is these hormones which we should be looking at, whereas what we are looking at now, sodium, potassium, calcium, are the incidental effects of these hormones and may not be the important factors related to blood pressure change.

Dr. Grossman:
Would either of our two speakers care to comment?

Dr. Langford:
I didn't hear Dr. Guyton yesterday, but I hear him frequently. We are from the same shop. I think his approach and yours are perhaps basically looking at the same thing. There are a number of homeostatic mechanisms. If you want to see a pronounced effect from one specific stimulus, what one can do is what Dr. Guyton's laboratory calls "locking" the other ones - infuse enough aldosterone, enough angiotensin, what have you, so that the normal homeostasis can't change, and then one can look at the effect of that specific nutrient. I would take it, though, that in general our problem here is not to look at these intermediate homeostatic mechanisms but at whether the primary stimuli are producing the change, and then it becomes a different order to find out what mechanisms are occurring or which are preventing it from occurring.

Dr. Sacks:
I agree.

Dr. Grossman:
A question that occurred to me while you were speaking, Doctor, is that all of these are acute effects. Do we know for certain that if these, let's call them insults, are repeated over long periods of time, that the body will find new homeostatic mechanisms for coping with them?

Dr. Langford:

May I answer one of these from the clinical vein, because it has been very attractive to think that changes in cortisol, which is the human analog of corticosterone, might be the cause of the alcohol-related hypertension. Garrett Beavers' work in Birmingham, England, suggests that this is not the case, although there are cortisol changes produced by very large alcohol intake. But that does not seem to be the critical mechanism for that important, I would agree with you, cause of hypertension which I hope some other meeting will addrss.

Dr. Grossman:

Well, of course this is of interest. The reason I raise the question is that people eat a lot of salt every day. You know, not a single intraperitoneal dose. People who drink alcohol may drink a lot everyday. The clinical correlates are, and I think there are many published papers that show that chronic alcoholism may breed hypertension, and in fact if you are successful in treating the chronic alcoholism, even if you do nothing else, the blood pressure will come down. Similarly, I was very struck a number of years ago, when several papers were published showing that if you said not a word to a group of obese people about their sodium intake, hammered at them until they got their body weight down to ideal body weight, their blood pressures came down. Of course, the objection was then raised that by cutting down on calories they also reduced their sodium intake. Did you want to have other comment?

Dr. Edozien:

Yes, I just want to respond very quickly to the question which you raised. Now, these acute experiments, in point of fact, yesterday I described an epidemiologic study we did in human populations. This study, using much greater analysis of the data, was what indicated to us which hormones were altered by each nutrient. These acute experiments were all designed to prove whether this was in fact the case. For example, in the epidemiologic study we saw that people on high carbohydrate diets had high levels of parathyroid hormone. So, we decided to see, if we gave acute injections of glucose, were we going to increase the parathyroid hormone? And that was about what happened. Nothing else but glucose would do it. And these were validations for the epidemiologic study. So, in response to your question, it does work like that in human populations on a nonacute basis.

Dr. Grossman:

Yes, thank you. Dr. Sacks, would you comment on either this topic and/or - you have a choice - why do you think vegetarians have lower blood pressures than nonvegetarians?

Dr. Sacks:

I just want to add one thing to what was said just recently. I think the interesting thing would be if there was a configuration of hormonal responses that might be adverse or beneficial irrespective of what happens to the blood pressure. That is being looked at, for example, in other fields, like in lipid metabolism, that a certain configuration of VLDL synthesis, or whatever. It doesn't matter what the level is, of VLDL in the blood, but is there a hormonal or metabolic state that is connected to blood pressure regulation that is itself adverse, and I think these are kind of interesting probes.

With regard to the vegetarians, I thought I really expressed my ignorance earlier this morning. I agree completely with the statement that Dr. Grossman made from the paper of Margetts, and I was hoping to be here this afternoon discussing dietary fat, but I cannot, unfortunately, but I just agree with that. We have done a number of studies, and so have others. You will hear another view later, but we have not seen changes in blood pressure with different amounts of dietary fat or different fatty acids. So I don't think it is that. It is a combination of two things. One is certainly the lower weight of the vegetarians; it is very important with gaining their low blood pressure. That is one thing, but that is not everything. The X factor - I don't know. What we are interested in is a combination of various cations. Vitamins could be important in some way, but we don't know. I think it is the fact that the vegetarians are eating a lot of cereal grains, a lot of vegetables and fruits as their main course, and they might have an accompaniment of some animal product. There is something about that, something in that which is favorable.

Dr. Grossman:

May I ask, when one of you in the audience asks a question, would you just start out by announcing your name.

Dr. Carter:

I have a question for Dr. Sacks which is a follow up on the question I asked earlier; then I have one for Dr. Langford.

There are vegetarians, and there are vegetarians. There are strict vegetarians and vegands, and they are not all the same. I was intrigued by the differences between your findings and the Australian findings. Your vegetarians were, I understand, primarily macrobiotic vegetarians. Now it has been our experience that the macrobiotic vegetarians consume a lot of salt. They consume pickles and special items in the Japanese dietary that are high in salt. You also mentioned that the Australian vegetarians may have had a higher intake of polyunsaturated fatty acids. Well, if in those polyunsaturated fatty acids, they were consuming gammalinolenic acid, which is a precursor of prostaglandin E1, which is a vasodilator, that may explain the fact that they got a drop in blood pressure and you did not. I can't remember if you said they also got a drop in cholesterol.

Dr. Sacks:

No, they didn't.

Dr. Carter:

They didn't get a drop in cholesterol. Okay. And that might also be related to the fact that their fat intake was higher. Could you respond to those questions? And then I have one for Dr. Langford.

Dr. Sacks:

Well, it is true, the macrobiotic vegetarians were influenced a lot by the Japanese people who started that diet - they based it a lot on Japanese eating patterns that are often pretty high in salt. They do eat a lot of salt.

The Seventh Day Adventists in Australia were not salt restricted - they ate a fair amount of salt as well. The interesting thing - I think what you are saying is that vegetarian diets are not vegetarian diets, are not vegand diets, etc., etc. This terminology is confusing; sometimes we ourselves blur these definitiions. I have called strict vegetarians strict vegetarians, even though they occasionally would eat some fish, and that is not right either, in terms of strict terminology. So I think we really ought to define what our terms are. But I think the interesting thing, the real contrast between the Seventh Day Adventists in Australia and the macrobiotics in Boston is that the diet, the Australian diet, does not lower cholesterol, and that is because they eat a lot of eggs. I think their dairy products are not restricted in fat. They have plenty of saturated fat. And there is something about this macrobiotic vegetarian diet that does both - it lowers blood pressure and it lowers cholesterol.

This idea about gammalinolenic acid - I just happen to agree with you that there are aspects of fatty acids that have not been that well investigated, and that particular aspect of a vegetarian diet, that certain vegetable products have a lot of gammalinolenic acid, really should be looked into, as the Omega 3 fatty acids should be. There is a lot of studies going on right now on Omega 3 fatty acids.

Dr. Carter:

The second question is about the apparent confusion on the effect of calcium. Could that be because we are talking about, on the one hand, intracellular calcium, which may be contributing to the hypertension, and on the other hand, we are talking about ionic calcium, sort of an immediate dose with an effect on the level of ionic calcium, which may have just the opposite effect. Those two are compatible - not necessarily incompatible.

Dr. Langford:

Sure, you have to have calcium for contraction, etc., but it doesn't really go right, Dr. Carter, for a high calcium to lower intracellular calcium, as near as I can tell, but I would extend my answer to your question, which your question didn't encompass it, to say that when we talk about calcium we need to specify whether we are talking about calcium intake, calcium excretion, total calcium in the blood, ionized calcium in the blood, and probably the level of the homeostatic hormones. Each of these may give you a different answer if you look at it this way.

Before I do this, I wanted to go into this vegetar-

ian thing to give Paul here the definition of being a vegetarian given by my son, Robert Langford's, best friend, a gal who says she never eats anything that was ever cute. That means she can have lobster but not lamb, shrimp . . . .

Dr. Howard:

Dr. Langford, getting back to this concept, that there may be a superiority in blacks at retaining sodium, and seeing the fact that this could tie into a survival concept of living in hot countries, and sodium retention being an important issue from sweat, have there been good studies that have looked at the sodium losses from sweat in the different races under the same conditions.

Dr. Langford:

The only study that I know of came from a very distinguished laboratory and it was very bad. It was from the Harvard Fatigue Group, World War II, and they came down to Mississippi to look at this. They found that the blacks, when put to a certain heat thing, were conserving sodium much more than whites. This, I am sure, was one of the most naive studies. Of course, it was before Jerry Kahn had done the study showing how you adapt to heat - one of your adaptations is lowering your sweat sodium. They got the white storekeepers and compared them to the black guys who were working, and they got a different answer. I think it was published in the American Journal of Medical Sciences, 1941, or something like that - a well-forgotten study.

I would like to say that, even though Dr. Grim participated in some of these studies showing different amounts of sodium conservation by blacks, I don't buy them at the moment. I would point out that just for certain times after you give the sodium load - my guess is that if we equalize, really equalize, for blood pressure and equalize for potassium intake, that these differences will be steadily attenuated. We have just completed a potassium loading study that I was telling Dr. Grim about. The blacks came in - these were moderate hypertensives studied by Cushman and Langford, Jackson V. A. Hospital - blacks came in excreting much less potassium, same sodium, the plasma-renin activity was much lower - very significantly lower. Eight weeks of potassium supplementation, 80 milliequivalents, the blacks' plasma renin activity came up to where the whites were; the whites didn't go up any more. All these homeostatic mechanisms should be examined only after very careful equilization of the whole situation, including the true blood pressure. Some of these studies, I think, are erroneous because they take several blood pressures from one group, say, "We will pick people with the same blood pressure and we will compare them." There are good statistical studies that show that you get different regression to the median when you pick subjects with different means, and so I don't think they are even comparing people with the same blood pressure. It may be so, but I find it unproven, and therefore I don't know that we have to sweat about finding the mechanisms of it.

Dr. Howard:

The data that were provided by Dr. Saunders suggested that thiazides might be especially beneficial in lowering blood pressure, particularly in blacks. Are there any of their effects on blood pressure that can be ascribed to other than just what they do to sodium, particularly, for instance, in terms of whether or not they might be blocking thermogenesis or other aspects of CNS activity? Would you discuss that briefly?

Dr. Langford:

This is a bit of a set question, thank you. We are doing a study which is a three by three design where we are looking at the effects of weight, sodium restriction, of thiazides and of B- blockers. The B-blockers substantially attenuate the efficacy of the weight lowering balance more than can be accounted for, I think, in terms of differences in sodium retention. The thiazides increase the efficacy of weight lowering more than you can account for by the diuretic. Now this goes along with the ideas that the catechol - induced thermogenesis is one of the factors affecting weight. And the thiazide treated person has higher catechols, steady state, all of the studies don't show this, but I think those with adequate sample size do. So they are being constantly hyperstimulated. I would put it that the B-blockers are being blocked from the thermogenic action, and the facts are as I gave you. The explanation you can buy or not. All of these drugs

that we give have complex effects.

Dr. Grim:
Clarence Grim, from Los Angeles. Vegetarians, in my book, tend to be kind of an odd lot. Maybe in Boston they are, and in Australia they certainly are. Odd lots tend to occur in families. Did you measure blood pressure in family members of vegetarians to see, if as a group, do they have lower blood pressures than in another random sample or family members of your control subjects?

Dr. Sacks:
That is an interesting question. No, I don't think we did. The Australians might have. It is interesting. I didn't mention this study that compared Seventh Day Adventists vegetarians in Australia with Mormon nonvegetarians in the same place. These were populations in Perth. It is interesting about odd lots - maybe there are odd lots and ex-odd lots. Some of the members of the Australian group were ex-Seventh Day Adventists.

Dr. Langford:
Or partially sliding . . .

Dr. Sacks:
Backsliders. Anyway, it is their impression that a virtually perfect control group, in terms of socioeconomic, religious adherence, all that, would be Mormons, who were nonvegetarian, to compare with Seventh Day Adventists, who were vegetarian. They organized a beautiful study, and it looked like their supposition was right, based on their objective - voluminous objective data about the populations. And the Adventists did have somewhat lower blood pressures, even after adjustment for the little differences that did occur. But I don't know about family studies.

Dr. Zemel:
Paula Zemel, from Detroit. My question is for Dr. Sacks. Can you hear me?

Dr. Sacks:
Yes.

Dr. Zemel:
Good. I guess I am an odd lot. I am a vegetarian and so is everyone else in my family. When I look at my own behaviors, in addition to not eating meat, there are other things that I do that could potentially confound my blood pressure - I don't smoke, I meditate, I exercise. Could you discuss those potential components.

Dr. Grossman:
Repeat the question, please.

Dr. Sacks:
The question relates to whether there are other healthy behaviors in vegetarians that would lower their blood pressure, or other things. It is certainly possible. To give you an example, the Seventh Day Adventists, particularly, are nonsmokers. They don't drink alcohol. And that could be important. That is one reason why they picked the Mormons to compare with, because they are much the same in that regard, and there is still a difference. The vegetarians I studied in Boston - about half of them were smokers, and the reason is the cultural influence from Japan, that in Japan they smoke a lot, and the leaders of the macrobiotics smoked a lot. The macrobiotics felt that their diet would protect them from any adverse effects of smoking. So, in one sense, they might have been worse off than other populations because half of them were smokers, and the time I studied them was before the physical activity boom, and there wasn't much in that way.

Dr. Langford:
May I give one reference? For anyone in the group who is interested in the sodium-potassium story, one of the sort of basal papers has just come out. Intersalt, a comparison of blood pressure, weight, sodium excretion, potassium excretion, and eventually they will report on calcium, magnesium, etc., in fifty populations throughout the world, has just been published in British Medical Journal a couple of months ago. It puts these things on as rigorous a quantitative epidemiological basis as you can. It does find a real role for sodium, which is considerably strengthened if you put in potassium. I advise all of you to read it very, very carefully. But it is not quantitatively a

very big thing. It is of public health importance. It is not of immediate patient treatment importance.

Dr. Grossman:
Thank you for your comments, and thank you all for being a wonderful audience. I am sure everyone here agrees that every answer to one of your questions leads to at least two more questions, and we could go on for the best part of the day. But we do have to quit - it is 12:00 o'clock, and we will see you all back here at 1:30. Thank you.

Fourth Scientific Session

Chair Lyn J. Howard, M.B., FRCP

PROTEINS AND AMINO ACIDS: INFLUENCES ON BLOOD PRESSURE REGULATION

G. Harvey Anderson
Departments of Nutritional Sciences and Physiology
and the Institute of Medical Sciences
University of Toronto
Toronto, Ontario

Introduction

The ingestion and digestion of food containing protein provides free amino acids to extracellular and intracellular fluids. Within cells, amino acids act either as substrate for protein synthesis or as precursors for the synthesis of many important small molecules.

Of considerable significance in the regulation of neuronal function are those amino acids which serve as neurotransmitter precursors and show acute changes in the nerve cell after food consumption. Because blood pressure is regulated by neurochemical systems which may be influenced by the availability of amino acids, it is logical to hypothesize that protein and amino acid ingestion influences the regulation of blood pressure. However, experimental data from studies involving humans have not supported this hypothesis.

To provide a perspective on the influence of protein and amino acids in blood pressure regulation this review is organized as follows. First described is how food proteins and amino acids affect the nervous system. Amino acid uptake by the nervous system, with primary attention given to the principle of precursor control of neurotransmitter synthesis, is reviewed. Second, the effect of single amino acids, or of modified protein diets, on blood pressure regulation in rats and humans is described.

Amino Acid Uptake by the Nervous System

Amino acids are readily transported across most plasma cell membranes by several major transport systems (1). In the brain, amino acid availability to nerve cells is influenced by the presence of tight junctions between epithelial cells in the capillaries. The presence of these tight junctions means that amino acids do not reach brain cells from the vascular system by diffusion between cells, as occurs in other tissues, but must be transported. Thus, brain amino acid concentration is relatively different from that of plasma.

Transport of amino acids across the blood-brain-barrier is achieved by means of three distinct systems (2). These systems are the L-system for the neutral amino acids, the basic system for lysine and arginine and the acidic system for aspartate and glutamate. Plasma concentrations of the large neutral amino acids approximate the km of their transport system so that the system is usually fully saturated. As a result, brain concentrations reflect both absolute and relative concentrations of large neutral amino acids in plasma. For example, when tyrosine, the amino acid precursor for the catecholamine neurotransmitters, was injected into rats, with an equimolar concentration of branched chain amino acids (valine, leucine and isoluecine), the competing large neutral amino acids reduced by 48 percent the maximal concentration of tyrosine in brain. In contrast, the presence of the branched chain amino acids had no effect on the concentration of tyrosine in plasma or tissues (3). The uptake of tryptophan by the brain is similarly reduced by increased plasma concentrations of the branched chain amino acids (4), and by phenylalanine or tyrosine (5).

Physiologically significant competition of amino acids for transport at the blood-brain-barrier occurs, not only after the injection of pure amino acid mixtures, but also after the consumption of protein. This occurs because the protein composition of the diet has marked effects on plasma and brain free amino acid concentrations (6). In general, the concentration of essential amino acids in food is reflected in plasma (7). The relationship between food and plasma concentrations is the most direct for the branched chain amino acids, which can be explained on the basis of both the composition of protein and the metabolism of amino acids. Branched chain amino acids comprise 10-20 percent of food proteins, being higher in animal proteins than in plant proteins. In contrast, amino acids such as tryptophan, phenylalanine and tyrosine, make up only approximately 0.8, 3.0, and 2.5 percent, respectively, of food proteins. The concentrations of these are the same or somewhat lower in plant compared with animal proteins. In addition to being present in foods in relatively large amounts, branched-chain amino acids are metabolized differently from other amino acids. Most amino acids are catabolized in the liver, whereas branched chain amino acids are catabolized primarily in the muscle (1). Thus while many plasma amino acids increase in rats fed high protein diets, those showing relatively large increases are the branched chains (8).

When an organism continuously consumes a diet which exceeds its protein requirements, the effect on plasma amino acids is buffered by the enhanced catabolism of amino acids by liver (the majority) and muscle (the branched chains). Thus, plasma amino acid concentrations are high in the first few days after a rat is placed on a high protein diet (9) but with time there is a gradual reduction in plasma concentration. This indicates that the animals increase their capacity to utilize excess dietary amino acids for energy production. Nevertheless, there is a sustained relationship between dietary protein levels and plasma amino acid concentration, with a strong positive association between protein intake and the plasma concentration of large neutral amino acids, especially valine, leucine, and isoleucine (7,8).

Because of amino acid competition for transport mechanisms, brain amino acid concentrations do not directly reflect those in food and plasma. For example, the relatively large increase in plasma branched chain amino acids in rats fed high protein diets for two weeks results in brain uptake of tryptophan and phenylalanine being reduced (8). On the other hand brain concentrations of the branched chain amino acids generally show a positive correlation with protein content of diets chronically consumed.

Amino acid uptake by innervated tissues other than the brain does not appear to be influenced by amino acid competition for the transport systems (3). Similarly, tyrosine availability to the adrenal chromaffin cells is not affected by the plasma concentration of large neutral amino acids (3,10). However the urinary excretion of catecholamines after tyrosine loads is directly correlated with plasma tyrosine concentrations (10). Therefore a protein meal, which raises plasma tyrosine levels, leads to an increase in tyrosine in the adrenal (6). The accumulation of tyrosine by the adrenal is of interest because it is specific for this large neutral amino acid, perhaps suggesting that preferential uptake of tyrosine is for the purpose of catechol synthesis.

Clearly, protein ingestion influences the availability of amino acids to the central nervous system and the sympathoadrenal system. Fluctuations in amino acid concentration in nerve and chromaffin cells are of interest because of the influence they may have on neurotransmitter synthesis (11).

Precursor Control of Neurotransmitter Synthesis

Amino acids known to function directly as neurotransmitters, such as glutamate, -aminobutyric acid, and aspartic acid, are dietary non-essential amino acids and metabolic controls within the neuron regulate their production and release for neurotransmission (12). However, fluctuations in tryptophan, tyrosine and histidine concentration in the brain influence neurotransmitter synthesis (11,12). In the case of tryptophan and tyrosine, this occurs because the hydroxylase enzymes, which catalyze the first step in the metabolic conversion of the amino acids to their respective neurotransmitters, are unsaturated at physiological levels of their substrates.

Until the 1960's it was assumed that the conversion of tryptophan to the active neurotransmitter, 5-hydroxytryptamine (serotonin) was independent of substrate availability. A clear indication, however, that brain tryptophan hydroxylase is unsaturated by normal brain tryptophan concentrations was provided when tryptophan injections were shown to increase brain serotonin content in rats that were pretreated with a monoamine oxidase inhibitor to block breakdown of serotonin to its inactive metabolite, 5-hydroxyindoleacetic acid (13). This observation led to further studies showing that large tryptophan loads increased brain content of both serotonin and 5-hydroxyindoleacetic acid (14). The demonstration of a precursor effect of tryptophan was recognized to be of physiological significance when it was shown that tryptophan injected intraperitoneally, in amounts as low as 12.5 mg/kg (approximately 5 percent of the rats' normal dietary tryptophan intake), would raise brain serotonin concentration and that food ingestion could also influence brain serotonin concentration (12). In recent years, many reports have verified the precursor effect of intraperitoneal injections or feeding of 25-200 mg/kg tryptophan on rat brain serotonin content (11,15).

Protein consumption also affects brain serotonin synthesis and concentration, consistent with the effect of protein on plasma neutral amino acid ratios and brain tryptophan uptake and concentration. The higher the meal is in protein concentration, the lower is the relative concentration of brain tryptophan and serotonin. Indeed, negative linear correlations are readily observed between meal protein to carbohydrate ratio and brain tryptophan and serotonin content by most investigators (15,16).

In humans, tryptophan consumption may also influence neurotransmitter synthesis. Increased cerebral spinal fluid levels of the serotonin metabolite 5-hydroxyindoleacetic acid have been found after tryptophan loads (17) suggesting enhanced serotonin turnover. Meals of protein (18) or tryptophan free amino acid mixtures (19) rapidly reduce plasma tryptophan concentrations in relation to the branched chain amino acids. However, there is no direct evidence available showing that serotonin synthesis is reduced.

The influence of tyrosine availability in free pools on catecholamine synthesis in neurons is not easily observed, possibly due to a more elaborate control system for catecholamine synthesis (11,12). Enhanced catecholamine turnover in brains of rats has been most readily observed after tyrosine administration when increased tyrosine availability is combined with activation of catecholamine neurons, such as occurs during cold exposure or following probenecid (12). Similarly, feeding may activate catecholaminergic neurons because when tyrosine was fed to rats in a meal of protein, increased hypothalamic norepinephrine turnover was indicated by an increase in 3-methoxy-4-hydroxyphenylethyleneglycol accumulation (20). However, prior activation of neurons may not always be necessary because tyrosine injected intraperitoneally has been shown to increase synthesis of brain catecholamines as well as the neurotransmitters, tyramine and octopamine (21) in otherwise untreated rats.

Several studies have shown that tyrosine consumption increases synthesis of the catecholamines in the human, although it is not clear whether the effects are both central and peripheral. Tyrosine consumption in amounts approximating normal dietary phenylalanine plus tyrosine intakes, or approximately 100 mg/kg, increases urinary excretion of the catecholamines (10) or of their break-down metabolites (22). In the latter study, the increased plasma concentration and urinary excretion of the norepinephrine metabolite, 3-methoxy-4-hydroxy-phenylethyleneglycol suggested that tyrosine was having an effect on the central nervous system. Consistent with a central effect of tyrosine is the finding that plasma free and conjugated forms of norepinephrine were decreased in young men consuming 7.5g of tyrosine daily for three days (23). A decrease in plasma norepinephrine is observed after central stimulation of noradrenergic neurons by drugs used to decrease blood pressure (24). Evidence for a central effect of tyrosine on dopamine synthesis in the human has been provided by the increase in the dopamine breakdown metabolite, homovanillic acid, in cerebral spinal fluid of Parkinsonian patients treated with tyrosine (100mg/kg) and probenecid (25). Thus, it might be hypothesized that the oral administra-

tion of tyrosine, by increasing the synthesis of brain catecholamines, would result in the stimulation of central catacholamine neurons with a resultant decrease in the release of NE by peripheral sympathetic nerves.

Amino Acids and Blood Pressure Regulation

Knowledge that the amino acids tryptophan and tyrosine can exert precursor control over the syntheses of neurotransmitters derived from them has stimulated considerable investigation into the functional significance of this relationship, as reviewed elsewhere (11). One function of catecholamine and serotonin containing neurons, is blood pressure regulation, thus raising the possibility that dietary protein and amino acid intake might influence blood pressure.

Evidence for a relationship between amino acids and blood pressure regulation has been provided from studies of the spontaneously hypertensive rat (SHR). Compared to the non-hypertensive control, the SHR shows a number of differences in plasma and tissue amino acid concentrations which may be related to the development and maintenance of hypertension (26). That is, plasma patterns in the SHR predict a reduced brain content of tryptophan and tyrosine, although this prediction has not yet been measured directly.

If brain tryptophan and tyrosine are low in the SHR, and if this is a factor influencing the development of hypertension, it might be expected that approaches which increase availability of these amino acids would result in a reduced blood pressure. When injected intraperitoneally, 200 mg/kg of tyrosine or tryptophan reduced blood pressure in SHR by 46 and 27 percent, respectively (4,27). In contrast, leucine, isoleucine, valine, alanine, aspartate and arginine had no effect. Tyrosine reduced blood pressure in the SHR, whether given either intraperitoneally (27), intraventricularly (28), or by prolonged infusion (29). Tyrosine feeding has a beneficial effect in slowing the development of hypertension in the DOCA-saline treated rat (30).

The favorable effect of tyrosine on hypertension in the SHR provided a strong indication that tyrosine might be a useful therapeutic substance in the treatment of essential hypertension in the human. When tested, however, the effects of tyrosine were disappointing (31). In this study, patients with mild essential hypertension consumed 2.5 g of tyrosine three times daily (approximately 100 mg/kg; twice the normal dietary intake) with regular meals for two weeks. Compared with two weeks of treatment with a placebo, there were no differences in systolic, diastolic and mean blood pressure, heart rate or plasma norepinephrine levels. Consistent with this suggestion is the observation that normotensive individuals receiving 7.5 g of tyrosine daily (2.5 g with each of three meals) for three days did not show any blood pressure response, even though plasma norepinephrine concentrations decreased (23). Possibly a study in patients with abnormal supine and standiung venous plasma norepinephrine would lead to more encouraging results. As pointed out earlier, it has been hypothesized that tyrosine administration should be more effective in neurons with increased firing frequency (12). Tryptophan administration (equal to 12.5 to 25 percent of the rats daily intake of tryptophan when on a 20 percent casein diet) also lowers blood pressure in normal and hypertensive rats (4,32). Similarly, in one clinical study tryptophan administration brought about a decrease in blood pressure in humans with essential hypertension (33). This was a single bolus study in which 50 mg/kg of tryptophan reduced both diastolic and systolic blood pressure 90 minutes later. Whether or not smaller amounts, approximately the normal dietary intake of tryptophan (15-20 mg/kg) taken on a sustained basis, will benefit individuals with essential hypertension remains to be determined. Normotensive individuals do not alter blood pressure after either a single bolus of 50 mg/kg (33) nor after three days of 3.0 gm daily taken one gram at each meal (23).

Protein Intake and Blood Pressure Regulation

The effect of protein composition and quantity on blood pressure in the human has been of interest primarily because lower blood pressure is found in ovalactovegetarians and vegetarians compared with meat eaters. At the present time there is no clear evidence that either quantity or composition of the protein consumed affects blood pressure independently of other dietary

components which are different in omnivore and vegetarian diets.

Ovalactovegetarian diets lower blood pressure. This benefit has been shown by studies in which the blood pressure of vegetarians has been compared with omnivores (34,35). Generally an advantage of 5-6 mm systolic or 2-3 mm Hg diastolic pressure is observed. Controlled intervention studies give the same picture. If either normotensive (36) or hypertensive (37) individuals are switched from omnivore to vegetarian diets, systolic pressure is decreased by 5-6mmg by six weeks.

Protein quality and composition is a major difference in the diets of vegetarians and omnivores. Vegetarians avoid meat, but also generally have lower protein intakes than omnivores (18). These factors, combined with early observations that consumption of milk and eggs is predictive of blood pressure levels in vegetarians (38,39) has lead to attempts to define the influence of protein on blood pressure regulation.

Changes in either quantity or composition of protein does not influence BP of vegetarians. For example, an increase in total dietary protein intake from 63 to 119 g/day, by adding a soy-wheat protein mixture to the diet of vegetarians, did not affect blood pressure (40). Similarly, the addition of meat (250 g/day) to the diet of vegetarians increased systolic blood pressure by 3 percent (41), but some have attributed this to increased stress due to a change in habitual diet to which the vegetarians were philosophically opposed.

Similar manipulations have been made in the protein content of the diets of normotensive omnivores. However, removal of animal protein produced no change in blood pressure when each subject served as his or her own control (40). In cross- sectional designs no differences were found in blood pressure when groups were given diets containing either 65 percent casein or 65 percent soy protein as a proportion of the total protein (42), or when virtually all the protein in a diet was provided by either meat (93 g/day) or by a vegetarian protein mixture (84 g) (43).

There is only one report suggesting that quantity of a specific dietary meal protein may relate to hypertension. In this report, populations with higher fish protein intake were found to have a lower incidence of hypertension than populations with lower fish protein intake (44) This benefit of fish consumption may, however, also be due to components of fish other than protein. An animal study in which spontaneously hypertensive stroke-prone rats were fed 50 percent protein diets containing protein from one of casein, cuttle fish, sardines or soy, failed to identify an effect of protein composition (44).

Although the current literature provides no evidence that either protein composition or quantity explains the lower blood pressure of vegetarians compared with omnivores, there remain research questions worth pursuing. First, it is possible that modification of protein intake and composition could be helpful in the treatment of hypertensive individuals, and this has not been tested. Second, measures of plasma amino acids and of eating patterns of omnivores compared with vegetarians would help elucidate factors related to protein intake which may be of physiological significance and relate to blood pressure.

Summary

Proteins and amino acids have the potential to influence many functions of the brain and the sympathetic-adrenal system by impacting on the synthesis of neurotransmitters which are influenced by the availability of their amino acid precursors. One of the functions regulated by precursor dependent neuro- transmitters is blood pressure. However, despite encouraging data from experiments in rats, experiments conducted with humans have shown little benefit to treatment of hypertension with amino acids. Similarly, available evidence shows that neither the composition nor the quantity of protein ingested is an independent risk factor in the development of hypertension. However, the role of quantity and composition of dietary protein in the treatment of hypertension remains to be determined.

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DIETARY FAT AND HYPERTENSION

James M. Iacono* and Rita M. Dougherty
U. S. Department of Agriculture, A. R. S.
Western Human Nutrition Research Center
Presidio of San Francisco, CA

Introduction

Hypertension is a well established risk factor for major cardiovascular disease and thus a great challenge to modern public health. Prospective studies show that an individual's risk increases with increasing blood pressure levels starting from levels so low that they are clinically considered normal (1). Since great numbers of people have slightly elevated blood pressure levels, the bulk of the risk attributable to hypertension is in this large segment of the population (2). The pharmacological reduction of blood pressure has to be restricted to people with overt hypertension and therefore the need for nonpharmacological control of elevated blood pressure, applicable to the large population groups at risk, is urgent. Several possible interventions have been proposed, including weight reduction, stress management, relaxation and dietary changes.

The role of nutrition in the control of blood pressure represents a challenge to scientists in the field of hypertension. For many years scientists have been concerned with the role of sodium in blood pressure regulation (3-5). In spite of all that has been accomplished, the role of sodium still remains controversial (6). A new and promising aspect of blood pressure regulation has been a series of studies that have implicated the role of dietary fat (7-26).

The studies reported in this paper will summarize the data in this field. Emphasis will be placed on seven different experimental nutrition studies performed at Beltsville, Maryland, USA, in North Karelia, Finland and a joint study performed in the USA, Finland and Italy. The results of these studies give strong support to the blood pressure lowering effect of dietary fat, specifically polyunsaturated fat (PUFA). A summary of the diets used in the different studies is given in Table 1 and a summary of the respective blood pressure results is given in Table 2.

Experimental Procedures and Results

Beltsville I

This study consisted of two 40-day periods (7). A seven-day dietary record was kept by each subject from which energy intake was determined. During the first experimental period all subjects ate a diet containing 25 percent of total energy as fat (en %) and during the second experimental period they ate a diet containing 35 en %. For both periods the polyunsaturated fat to saturated fat ratio (P/S) was 1.

Diet Composition

The food consumed in these experimental diets was commonly available in supermarkets and consisted of meats, poultry and fish along with a variety of fresh fruits and vegetables, cereals, pasta and other grain products. The diets were prepared on a meal-to-meal basis for each subject throughout the study and were intended to be typical of the USA. During the experimental periods calories from carbohydrates were substituted for calories from fat when the diet provided 25 en % as fat. The protein levels and general composi-

* Presenter

tion of the diets were similar in both experimental periods (Table 3).

Salt (NaCl) intake averaged between 9.2 and 10.3 g/day for both periods. If body weight changed, food intake was adjusted in 400-calorie increments to maintain body weight.

Blood Pressure

No attempt was made to select the subjects on the basis of their blood pressure. Systolic and diastolic blood pressure declined for both men and women during the first experimental period ($p < 0.05$) and did not change during the second experimental period (Table 2). During the first period, a significant decrease of about 12 percent for men ($p < 0.025$) compared to a 5 percent decrease for women was observed for both systolic and diastolic blood pressure. One month after the second experimental period the diastolic blood pressure increased slightly above the baseline level for both men and women while systolic blood pressure approached the baseline levels.

Beltsville II study

This study consisted of three periods with a switchback and cross-over design (14, 16-18). A seven-day dietary history of food intake of each subject was recorded. The first 21 days was a baseline period when all subjects consumed a 44 en % diet with a P/S of 0.3. Two 30-day periods followed. Ten subjects with diastolic blood pressure greater than 88 mmHg (hypertensive group) were fed a 25 en % diet (P/S 1), intervention period for 30 days, while ten subjects with a diastolic blood pressure less than 88 mmHg (normotensive group) continued on the 44 en % diet (P/S 0.3) switchback. At the end of the intervention period the two groups of subjects were switched from one diet to the other.

Diet Composition

The composition of the diet was similar to that in the Beltsville I study (Tables 1, 3), but some foods, especially eggs and dairy products were added to increase the fat content to 44 en% and to maintain a P/S of 0.3. As in the Beltsville I study, the diets were prepared by dietitians and all food was weighed and measured for each subject.

On both diets, daily NaCl intake was 10.5 g. During the baseline period salt was provided in weighed shakers and used ad libitum. The subjects consumed less salt during the baseline period than during the intervention and the switchback periods.

Blood Pressure

In the hypertensive group, systolic and diastolic blood pressures decreased significantly during the 25 en %, P/S 1 (Fig.1). When these subjects were placed on the 44 en %, P/S 0.3 diet during the switchback period, systolic and diastolic blood pressures increased significantly. Throughout the study, neither systolic nor diastolic blood pressure changed significantly in the normotensive group.

Beltsville III study

In this study, four groups of men consumed diets having two fat levels, 43 en % and 25 en %. Both of these fat levels were further subdivided into P/S 0.3 and 1.0 (20, 21). A one-week dietary history was recorded (baseline period) and the subjects were then placed on a stabilization diet for three weeks followed by one of the four diets for a six-week period. The diets were similar to those used in the Beltsville I and II studies (Tables 1, 3). The NaCl intake was 8.1 g and 8.6 g for the 25 en % and 43 en % diets, respectively.

Blood Pressure

Throughout the six-week study period and regardless of the fat content of the diet, the systolic and diastolic blood pressures were lower ($p < 0.04$) in the subjects on the P/S 1.0 than for the subjects on the P/S 0.3 diet.

Joint Study - USA, Finland and Italy

A cross-sectional epidemiological pilot study was carried out in Beltsville, Maryland, U. S. A.; Nurmijarvi, Finland; and Canino, Italy (15). Finland is a country with high cardiovascular disease rates and Southern Italy an area with low CVD rates. From each area, data were collected on farmers aged 40 to 45 years. All food was weighed for seven days and the diet composition was calculated (Table 4). Local dietitians visited the home of each subject and worked with the families to determine their food intake. Random dai-

ly food samples were also collected and analyzed.

Diet Composition

The total fat in the diet was at a level of 32 en % in Italy and 40 en % in the USA and Finland. The level of dietary saturated fatty acids was highest in Finland and lowest in Italy. The level of dietary linoleic acid was lowest in Italy and highest in the USA. The P/S was lower (0.16) in Finland than in Italy and the USA, 0.25 and 0.28 respectively. Alcohol intake differed markedly among the three areas. The Italians consumed 14 percent of their calories as alcohol, primarily as wine. The Finns and Americans reported about 1 percent of their total energy intake as alcohol.

Blood Pressure

Both systolic and diastolic blood pressures were significantly higher among the Finns than among either the Italians or Americans (Table 4).

North Karelia I Study

This study was conducted in the community of Liperi in North Karelia, Finland (17 - 19, 23, 24). Prior to the six-week intervention period, a seven-day dietary history was recorded by each subject, and the energy intake determined. During the intervention period all subjects (30 men and 29 woman, age 40-50 years) consumed a low fat diet with a high P/S (Table 2). Thereafter, during a six-week switchback period all subjects consumed their usual diet which contained 36 en % (P/S 0.16). All participants were instructed to eat sufficient food to maintain body weight. Body weights did not change significantly during the study.

Diet Composition

The foods eaten by the participants during the study were commonly available in North Karelia, Finland, and were typical for the area. During the intervention period high fat containing food items such as milk, cheese, meat, and sausages were replaced by similar items containing less fat. Margarines and oils prepared from sunflower seeds were substituted for butter and other cooking fats to increase the P/S of the diet. The estimated daily salt intake was 10.2 g, 11.9 g and 11.5 g for the three study periods.

Blood Pressure

Systolic and diastolic blood pressure were significantly lower during the intervention period than during the switchback period ($p < 0.0001$). The data obtained for blood pressure in this study were similar to those obtained for the Beltsville II study.

North Karelia II study

This study was conducted in two communities, Juuka and Lieksa in North Karelia, Finland (23). A total of fifty-seven families were identified from the local community-based hypertension register that functions in North Karelia (27). The participants, husbands and wives, were 30-50 years old and had no major health problems and were not being treated with antihypertensive drugs when they entered the study.

The families were randomly allocated to three different groups. During the intervention period, Group 1 consumed a low fat diet with a high P/S; Group 2 ate a diet typical for the region but low in sodium; and the third group did not change their usual diet (control group). The study consisted of three periods: baseline (two weeks), intervention (six weeks) and switchback (four weeks). During the baseline and switchback periods all the families were asked to eat their usual diets. During the intervention period the families in Groups 1 and 2 were asked to consume their respective experimental diets and the families of the control group were asked to continue with their usual diet. Except for the alterations in the diets, the families made no other changes in their lifestyles, e.g., smoking or exercise, throughout the study.

Diet Composition

The composition of the diets consumed in this study was similar to that in the North Karelia I study. Group 1 substituted low-fat food items for the usual high fat items and consequently reduced the total fat from 39 en % to 23 en % during the intervention period. During the switchback period the fat intake increased to 37 en %. The P/S were 0.27, 0.98 and 0.29, respectively. The en % from fat remained the same (39 en % with a P/S of 0.29) in the other two groups. Group 2 was asked to reduce their salt consumption during the intervention period to less than half their usual

intake. The families were provided with a number of low salt products, and were also advised by the dietitians to avoid salty products. They were asked, also, to prepare their food with a special low sodium salt and not to add salt to the foods at the table.

Blood Pressure

The mean blood pressure values for the last week of each period in the three groups are shown in Table 2 and Figures 2 and 3. During the intervention period, the systolic blood pressure decreased 8.9 mmHg ($p < 0.001$) and the diastolic pressure decreased 7.6 mmHg ($p < 0.001$) in Group 1, and during the switchback period systolic blood pressure increased ($p < 0.001$). Blood pressure changes in the other two groups were small and were parallel to each other. Diastolic blood pressure decreased only slightly in both groups ($p < 0.01$) and remained at the lower level during the switchback period. The results were similar for men and women.

North Karelia Study III

This study was conducted in two semirural communities, Kitee and Tohmajarvi, in North Karelia, Finland (25). A total of 84 middle-aged subjects (mainly couples) were identified from the local community-based hypertension register and through local risk factor screenings. The ages of the subjects were 35 to 49 years. They were borderline or mildly hypertensive, but had no major health problems and were not on antihypertensive treatment. The couples were randomly allocated to two groups. After a baseline period of two weeks on a 38 en % fat diet, P/S 0.2, they were switched to a diet containing 24 en % fat. One group consumed a high P/S diet, 0.9, and the second group consumed a diet with a P/S of 0.4. These lower fat diets were consumed for 12 weeks. At the end of the 12-week intervention period, the subjects returned to their usual diets for five weeks.

Diet Composition

The composition of the diets consumed in this study was similar to those eaten in the North Karelia I and II studies. As in previous studies in North Karelia, the intervention diet was accomplished through intensive counselling by dietitians. The lower fat intervention diet was achieved by substituting low-fat food items for several high fat food items similar to the previous studies. The difference in the P/S of the two intervention diets was achieved by providing a different fat spread for the two groups on a single-blind basis: one group used margarine high in polyunsaturated fats (mainly from sunflower oil), while the second group used a mixture of butter and margarine, specially prepared for this study.

Blood Pressure

The mean blood pressure values at the end of the study periods are shown in Table 2. As in the previous studies, systolic and diastolic blood pressures were reduced during the intervention period and increased toward initial levels during the switchback period. As in the second study conducted in North Karelia, the blood pressure decreased more in subjects with initally elevated blood pressure than among normotensives. No significant differences in blood pressure were observed between the two groups.

Discussion

The series of dietary intervention studies reported here demonstrate that blood pressure can be decreased or increased in hypertensive individuals by altering the fatty acid composition of the diet. Significant alterations in systolic and diastolic blood pressures occurred as a consequence of changing the dietary fat and took place within four to twelve weeks in both men and women. Mean blood pressure levels of the various groups dropped gradually during the course of the intervention periods. The full benefits and the long term implications of this type of dietary change are not known.

In view of the direct relationship between blood pressure and body weight (28, 29), body weights of the participants were maintained relatively constant in the various studies by adjusting calorie intakes. We can, therefore, rule out body weight as a factor affecting the changes observed in blood pressure in this series of experiments.

No attempt was made to alter salt intake, except in Group 2 in the North Karelia II study. An average of about 10-12 g/day was consumed in the

Beltsville and the North Karelia studies. The values obtained for 24-hour urinary Sodium excretion were essentially the same as the Sodium intake values derived from direct chemical analysis of the diet. We conclude that the level of dietary Sodium was not a factor in the blood pressure changes observed.

It was shown in the North Karelia II study that reducing dietary Sodium intake by about 60 percent in one group of hypertensive subjects caused only small changes in blood pressure compared to the dramatic change observed in the group consuming the low fat, high P/S diet. Salt intake and its relationship to blood pressure is controversial and requires a great deal more research.

High levels of dietary calcium have been reported to reduce blood pressure in animals and man (30). Because of the high consumption of dairy products, the intake of calcium in North Karelia, Finland was high (1.4 g per day). In spite of this, the blood pressure of the population of North Karelia remained relatively high suggesting that other dietary factors play a more important role in regulating blood pressure than dietary calcium. Calcium intakes did not change significantly during the different periods of the North Karelia studies.

The role of potassium in regulating blood pressure is also unclear. Available data suggests that a higher intake of potassium may reduce blood pressure, especially when the Sodium intake is high (31, 32). In the experiments by our group, this possibility could not be ruled out. For instance, in the North Karelia II study, potassium intake tended to increase somewhat during the intervention period (23), but it remained at the higher level when the subjects resumed their usual diets in the switchback period when blood pressure increased.

In seeking an explanation for the reduction of blood pressure in the studies reported, current data suggests that linoleic acid is the active nutrient. Animal and human data support this hypothesis (33). The mechanism of action of linoleic acid appears to be through its conversion to the prostaglandins, PGE_2 and PGI_2 which in turn have been shown to affect blood pressure (34-36). The first epidemiological evidence linking dietary linoleic acid intake to urinary Sodium excretion was reported by Oster et al. (9) where a significant positive correlation between these two factors was found. A more recent epidemiological study implicates ‡-linolenic acid in blood pressure control (37).

A preliminary report from our laboratory (26) lends support to the concept that dietary linoleic acid is the active nutrient that reduces blood pressure in man. In a study conducted in our metabolic unit where dietary saturated and monounsaturated fatty acids were maintained at 10 en % each and linoleic acid was fed at either 3 en % or 10 en %, we observed blood pressure reduction in hypertensive subjects when they consumed the 10 en % linoleic acid diet, but observed no change in blood pressure of the normotensive subjects.

Other studies supporting the linoleate effects on blood pressure include those of Comberg et al. (38), Rao et al. (11), and Fleishmann et al. (39). Studies conducted in vegetarians reviewed by Rouse and Beilin (40), and Beilin (41) also support blood pressure lowering effects of diets. One can speculate that an important nutrient maintaining the low blood pressure in vegetarians is linoleate since this group tends to eat more linoleic acid-containing foods, such as oils and nuts than non-vegetarians. The studies of Brussaard et al. (42) in young men and of Margetts et al (43) in the 20-59 age group did not show the dietary effect of linoleate on blood pressure. This may be due to the fact that they studied subjects whose blood pressure were in the normal range and were not significantly lowered through dietary intervention.

The biosynthesis and urinary excretion of prostaglandin derivatives related to different linoleate intakes for short time periods was reported by Adam et al. (44) and by Adam and Wolfram (45). These authors showed increased urinary excretion of creatinine, sodium, and total body prostaglandins and renal PGE in women after feeding various levels of linoleic acid. These data support the assumption that linoleic acid intake stimulates PG synthesis in the total body and in kidney which may lead to a reduction in blood pressure.

There are still many unanswered questions to be resolved in this field. Much research needs to be done to understand the role of various nutrients on blood pressure regulation before dietary recommendations can be made to the general

public. However, the emerging findings concerning the association between dietary fat and blood pressure seem to support the already existing dietary recommendations for modification of serum lipids in the prevention of cardiovascular disease.

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Table 1
Studies on the effect of dietary fat on blood pressure
Calculated composition of daily nutrient intakes[1] in five intervention studies (Beltsville I-III and North Karelia I-III).

	Protein	Carbo-hydrate	Fat	Saturated fatty acids	Linoleic acid	P/S ratio	Dietary cholesterol (mg)
	(% of total energy)						
BASELINE PERIOD							
Beltsville							
I	17.9	39.9	41.6	17.2	3.8	0.22	502
II	16.7	42.1	40.9	14.9	5.3	0.38	528
III	17.0	42.0	43.0	18.3	5.6	0.30	754
North Karelia							
I	13.6	48.7	38.6	21.9	3.1	0.15	541
II Control	14.7	46.7	37.2	19.1	4.4	0.25	479
Low Salt	14.9	44.3	38.4	20.2	3.9	0.21	498
Low Fat	15.3	44.4	38.6	19.5	4.7	0.27	475
III Group I	15.0	46.0	38.0	20.0	4.0	0.2	460
Group II	15.0	47.0	38.0	20.0	4.0	0.2	533
INTERVENTION PERIOD							
Beltsville							
I	15.7	60.0	26.4	6.9	6.5	0.95	185
II	15.7	59.8	26.4	6.8	6.6	0.98	270
III A	16.0	61.0	25.0	10.1	3.4	0.3	366
B	16.0	61.0	25.0	6.5	6.5	1.0	283
C	17.0	42.0	43.0	18.3	5.6	0.3	754
D	16.0	42.0	43.0	11.8	11.5	1.0	635
North Karelia							
I	17.5	59.7	23.6	7.6	8.5	1.2	301
II Control	14.7	45.7	38.0	9.5	4.3	0.24	500
Low Salt	15.1	44.8	38.1	21.4	3.4	0.17	581
Low Fat	21.4	53.9	23.3	6.9	6.4	0.98	282
III Group I	19.0	58.0	22.0	8.0	7.0	0.9	283
Group II	19.0	56.0	23.0	10.0	4.0	0.4	351
SWITCHBACK PERIOD							
Beltsville							
II	17.2	39.5	44.2	18.4	5.3	0.28	845
North Karelia							
I	14.2	50.6	35.9	20.1	2.5	0.16	539
II Control	14.3	45.9	37.8	19.3	4.3	0.24	446
Low Salt	14.9	43.8	39.5	21.2	3.8	0.19	508
Low Fat	15.5	46.7	36.8	18.4	4.7	0.29	470
III Group I	15.0	47.0	37.0	19.0	4.0	0.2	474
Group II	15.0	46.0	37.0	19.0	4.0	0.2	535

[1] Calculated from data in USDA Handbook No. 8 and Finnish Food Table.

Table 2
Mean blood pressure values (± SEM; mmHg) related to modified fat diets in the studies Beltsville I-II and North Karelia I-III

	n	Baseline period	Intervention period	Switchback period
BELTSVILLE I	21			
Systolic		136±4	123±3	129±3
Diastolic		80±3	73±2	83±2
BELTSVILLE II				
Normotensive group	10			
Systolic		132±3	123±4	120±4
Diastolic		87±2	81±4	81±2
Hypertensive group	10			
Systolic		145±6	126±4	137±4
Diastolic		99±5	88±3	93±4
NORTH KARELIA I	59			
Systolic		125±2	117±2	125±2
Diastolic		77±1	74±1	80±1
NORTH KARELIA II				
Reference group	38			
Systolic		138±2	136±2	138±2
Diastolic		89±2	87±2	88±2
Group I	35			
Systolic		138±3	130±2	137±2
Diastolic		89±2	81±1	85±2
Group 2	34			
Systolic		139±2	137±3	138±3
Diastolic		90±2	87±2	86±2
NORTH KARELIA III				
Group 1	41			
Systolic		128±2	124±2	129±3
Diastolic		88±1	82±2	85±2
Group 2	43			
Systolic		126±2	123±2	126±2
Diastolic		86±2	82±2	85±1

Table 3
Calculated nutrient composition of food eaten in the study - Beltsville I, average daily intakes.[1]

Constituents	Baseline period	First experimental period	Second experimental period
		en %	
Protein	17.9	15.7	15.8
Carbohydrate	39.9	60.0	49.4
Fat	41.6	26.4	36.5
Saturated fatty acids	17.2	6.9	9.7
Oleic acid	16.5	9.9	13.2
Linoleic acid	3.8	6.5	9.2
P/S ratio	0.22	0.95	0.97
Cholesterol, mg	502	185	306

[1] Calculated from data in USDA Handbook No. 8.

Table 4
Calculated composition of diets [1] and blood pressure mean values (ÒSEM; mm Hg) of subjects in a joint study - USA, Finland, Italy.

	Beltsville USA (n = 20)	Nurmijarvi Finland (n = 29)	Canino Italy (n = 17)
		en %	
Constituents,			
Protein	15	14	13
Carbohydrate	46	47	49
Fat	40	39	32
Saturated fatty acids	17.4	24.2	8.7
Linoleic acid	4.9	3.9	2.2
P/S ratio	0.28	0.16	0.25
Blood pressure, mm Hg			
Systolic	124±1	136±3	125±2
Diastolic	78±1	90±1	80±2

[1] Calculated from data in USDA Handbook No. 8

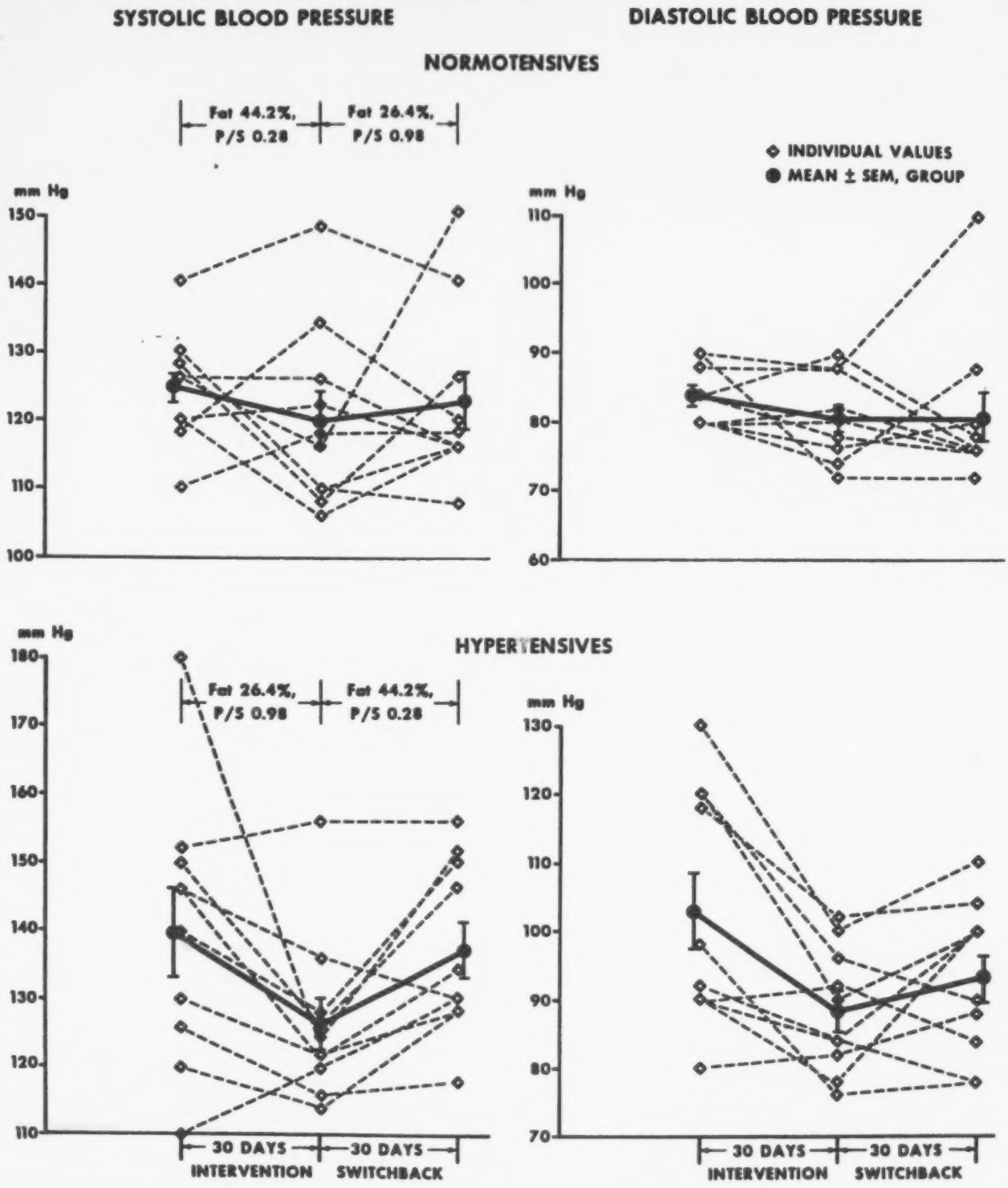

Figure 1: Blood pressure vaslues in the normotensive and hypertensive groups at the end of each dietary period in Beltsville II study

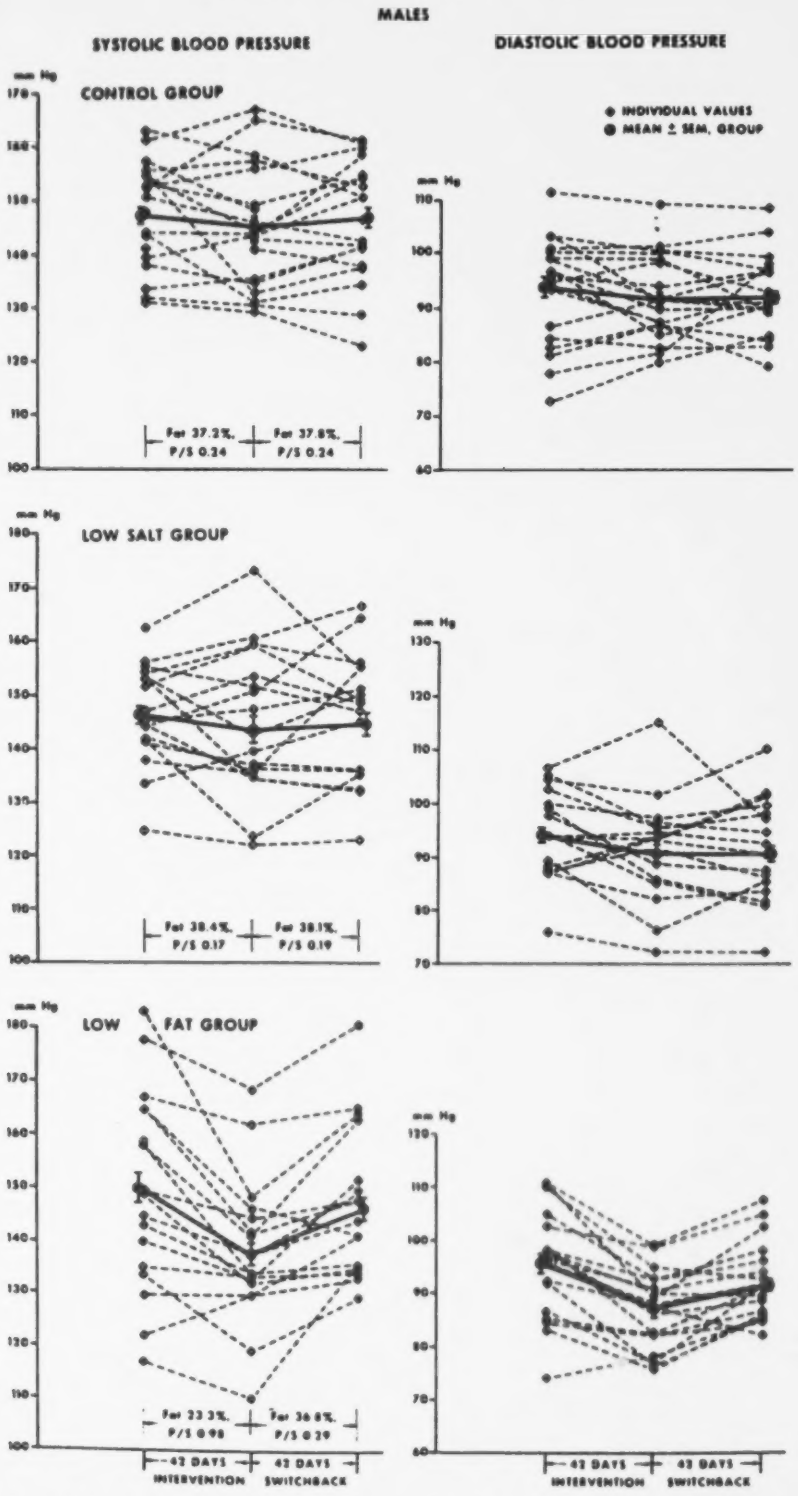

Figure 2: Individual blood pressure values at the end of each dietary period for men in the North Karelia II study.

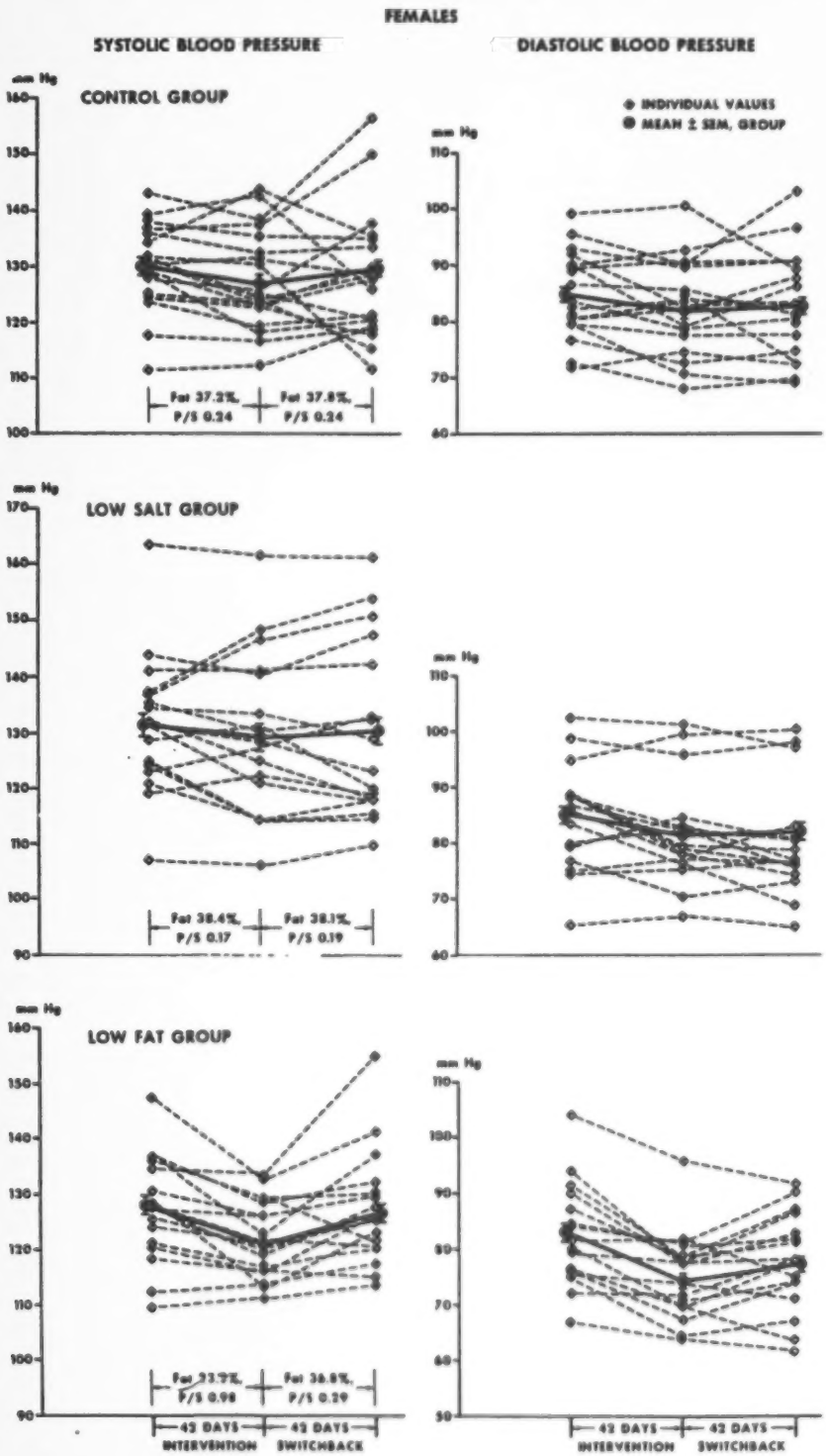

Figure 3: Individual blood pressure values at the end of each dietary period for women in the North Karelia II study.

OBESITY TYPE, RACE, GENDER AND HYPERTENSION

Osman Ahmed
Department of Internal Medicine
and Center for Nutrition
Meharry Medical College
Nashville, TN

Hypertension can be defined as a persistent elevation of blood pressure above "normal" levels. But what is high or "abnormal" blood pressure? Table (1) shows recently recommended standard or cutoff points that imply varying degrees of disease severity. Table (2) displays blood pressure levels in children and young adolescents. Since hypertension is related to atherosclerosis or "hardening of the blood vessels" and as the latter is an age related phenomenon, the development of hypertension is considered to be age related.

Atherosclerosis starts early in life and advances with increasing age (1,2). Women lag behind men during their reproductive years, but catch up after menopause.

Racial differences in atheriosclerosis are well documented. Data from Baltimore and Minneapolis have shown that blacks have a greater degree of atherosclerosis of the Circle of Willis (3). However, cerebral atherosclerosis was less frequent and less severe among Nigerian and Ugandan deaths compared to blacks in the U. S. A. (3-5). According to the United States Vital Statistics, hypertension is much more prevalent in blacks than whites in 1976-1980 in all age groups (Table 3). Large racial differences are observed in the 35-44 and 55-64 year age groups. Excess morbidity among blacks in these two age groups may be due to younger age of onset of hypertension (in the 35-44 age group) and lower proportion of effectively controlled hypertensives (in the 55-64 age group) in blacks than whites (6,7). The proportion of controlled hypertensives is generally lower in blacks than whites (Table 4).

Body Weight and Age

The Framingham study showed a clear relationship between relative weight and blood pressure for all age-sex groups (8). This relationship was found to be consistent in all age groups (Figure 1). Moreover, it is believed that the increase in blood pressure with aging may simply reflect the increased obesity in an aging population. Analysis of information from the First National Health and Nutrition Examination Survey (HANES) has suggested that it is central or truncal obesity (as measured by subscapular skinfolds) rather than peripheral fat (as measured by triceps skinfolds) that best predicts hypertension (9). Table 5 shows that subscapular skinfold is correlated with blood pressure levels to a higher degree than triceps skinfolds. The observed variation in blood pressure due to inclusion of the triceps skinfolds is least pronounced than the subscapular skinfolds.

The relationship between obesity and blood pressure is probably a dynamic one. Stamler (10) using tailored dietary modification that included a restricted caloric intake for 78 known obese hypertensives achieved a significant reduction in both body weight and systolic and diastolic blood pressure observed even after 4 years. The average drop in diastolic and systolic blood pressure was between 5 and 10 mm Hg respectively and the mean reduction in body weight was 4 pounds. Findings of the Meharry Cohort Study (11) support this hypothesis when body weight and blood pressure of 433 medical students were measured twice at the initial evaluation and at followup after 23 years. Weight gain was more contributory

to the development of hypertension than initial body weight or weight at the end of the study period (Tables 6,7).

Despite the overall higher prevalence of hypertension in blacks than whites, mortality data indicate a decreasing ratio of black/white mortalities due to hypertension (12). This was accompanied by a reduction in the black minus white mean blood pressure (Table 8). In addition, data from five community surveys indicate a reduced black/white odds ratios for prevalence of hypertension (Table 9).

Socioeconomic Status and Hypertension

According to the Hypertension Detection and Followup Program (HDFP), there is a significant inverse association between relative weight, hypertension, and duration of formal education (13,14). The relationship was much more striking for blacks than whites and persisted even after adjustment for body weight. Similar findings came from the 1981 survey of representative samples of Georgia households (15). Income was significantly lower among individuals with moderate or severe hypertension than in those where hypertension was mild or controlled. This applies to all sex-race groups except white women.

In addition, analysis of the HDFP data has demonstrated an inverse association between education and five-year mortality in white men (16). The less educated black men are at 1.4 to 4 times higher risk of dying compared to white men with the same or higher education (Table 10).

International Comparisons

Hypertension was reported to be uncommon in many rural communities in Kenya (17), Uganda (18), and Tanzania (19). Epidemiological studies in Ghana have shown that rural Ghanains have much lower blood pressure and less steep increase by age compared to U. S. blacks (20). Joossen reported similar findings in other primitive communities with virtually no age change in blood pressure (Table 11. This is in contrast to more urbanized, industrialized communities where higher levels of blood pressures were reported (Table 12). Possible explanations are that members of primitive or tribal communities do not gain weight as they age, they remain physically active and they consume less fat and meat, more vegetables and fiber, as well as more potassium and less sodium.

Migrant studies provide more evidence for the environmental influence on hypertension. The prevalence of hypertension among U. S. Japanese is higher than among Japanese in Japan (Table 13). However, the blood pressure of Japanese in Hawaii and California are similar to those of the U. S. whites (21). Part of the difference may be related to a greater prevalence of obesity among U. S. Japanese.

Since hypertension is the cardinal risk factor for stroke, much more helpful information could be obtained by studying stroke in various ethnic groups. Stroke death rates are not elevated among the Japanese, Korean, and Phillipines compared with U. S. whites or blacks (Table 14). However, stroke mortality rates among blacks are not limited to the United States. In Lagos, cerebrovascular accidents were the second most common cause of all neurological admissions in the sixties. In Ibadan, Nigeria, the incidence of stroke was 26/100,000 in 1983. However, ischemic heart disease is still fairly uncommon (21). The picture in Africa and especially in urban areas is very similar to the United States many years ago.

Despite the declining trend in hypertension and hypertension related mortalities, hypertension is still responsible for 30,700 deaths annually in the U. S. (22) The annual cost of hypertension is $11 billion. According to the 1988 Heart Facts (22), 60 million Americans are currently suffering from hypertension.

In conclusion, more detection and control of hypertension is needed especially after the success of the HDFP. Understanding the interactions of risk factors for hypertension and international comparisons of the disease rates and risks are invaluable for instituting more vigorous control campaigns in the United States and worldwide.

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Table 1
Classification of Blood Pressure

Range (mm Hg)	Category*
Diastolic	
<85	Normal BP
85–89	High normal BP
90–104	Mild hypertension
105–114	Moderate hypertension
⩾115	Severe hypertension
Systolic, when diastolic BP is <90	
<140	Normal BP
140–159	Borderline isolated systolic hypertension
⩾160	Isolated systolic hypertension

Source: From Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure, 1984, with permission.

*A classification of borderline isolated systolic hypertension (systolic BP, 140–159 mm Hg) or isolated systolic hypertension (systolic BP, >160 mm Hg) takes precedence over a classification of high normal BP (diastolic BP, 85–89 mm Hg) when both occur in the same person. A classification of high normal BP (diastolic BP, 85–89 mm Hg) takes precedence over a classification of normal BP (systolic BP, <140 mm Hg) when both occur in the same person.

Table 2
Suspect Blood Pressure Levels in Children and Adolescents

Age group	Blood pressure (mm Hg)
3–5	⩾110/70
6–9	⩾120/75
10–13	⩾130/80
14–19	⩾140/85

Source: Adapted from S Londe and D Goldring: Am J Cardiol 37:650, 1976, by permission of the American Heart Association, Inc.

Table 3
Age-specific and overall prevalence of elevated blood pressure in black and white men ages 25-74, United States, 1976

	rate per 100 population with elevated blood pressure**					
Age-group	25-34	35-44	45-54	55-64	65-74	Total
Black Men	11.7	22.3	23.0	39.2	27.5	22.4
White Men	8.4	10.6	21.2	22.3	24.5	15.9
Black minus White	3.3	11.7	1.8	16.9	3.0	6.5

* from Reference 1, Table 5
** defined as SBP >=160 mmHg and/or DBP> >=95 mmHg

Source: Report of the Secretary's Task Force on Black and Minority Health, Vol IV: Cardiocascular and Cerebrovascular Disease, Part 2, 1986.

Table 4
Prevalence rates of hypertension of persons 25-74 years of age by treatment history, race, and sex, with standard errors of percent: United States, 1960-62, 1974-75, and 1976-80.

Race and sex	Hypertensive[1]			Never diagnosed[2]			On medication			On medication and controlled[3]		
	1960-62	1974-75	1976-80	1960-62	1974-75	1976-80	1960-62	1974-75	1976-80	1960-62	1974-75	1976-80
	Percent of population[4]			Percent of total with hypertension[1,4]								
All people 25-74 years[5]	20.3	22.1	22.0	51.1	36.4	26.6	31.3	34.2	56.2	16.0	19.6	34.1
White men	16.3	21.4	21.2	57.6	42.3	40.6	22.4	25.9	38.3	11.8	15.1	20.9
White women	20.4	19.6	20.0	43.9	29.7	25.2	38.2	48.5	58.6	21.9	28.1	40.3
Black men	31.8	37.1	28.3	70.5	41.0	35.7	18.5	24.0	40.9	5.0	12.7	16.1
Black women	39.8	35.5	39.8	35.1	28.9	14.5	48.1	36.4	60.6	20.2	22.3	38.3

[1]Elevated blood pressure (that is, a systolic measurement of at least 160 mm Hg or a diastolic measurement of at least 95 mm Hg) or taking antihypertensive medication.
[2]Reported never told by physician that he or she had high blood pressure or hypertension.
[3]Subset of "On medication" group: those taking antihypertensive medication whose blood pressure was not elevated at the time of examination.
[4]Age adjusted by direct method to the population at midpoint of the 1976-80 National Health and Nutrition Examination Survey.
[5]Includes all other races not shown separately.

Source: Adapted from Rowland M, Roberts J: Blood pressure levels and hypertension in persons 6-74 years: United States, 1976-80. National Center for Health Statistics, U.S. Department of Health and Human Services, Public Health Service. Advance Data 84 1982, table 7.

Table 5
The variance in blood pressure explained by subscapular and triceps skinfold by stepwize regression. (HANES, 1971-1974, ages 30-59)

Race-sex group	Sample no.	% of total variance explained ($R^2_{1,23}$)	Stepwise regression: Subscapular skinfold added first — % variance explained by subscapular skinfold alone ($R^2_{1,4}$)	Stepwise regression: Subscapular skinfold added first — Variance added by triceps skinfold ($r^2_{2,3,4}$)	Stepwise regression: Triceps skinfold added first — % variance explained by triceps skinfold alone ($R^2_{1,3}$)	Stepwise regression: Triceps skinfold added first — Variance added by subscapular skinfold ($r^2_{2,3,4}$)
Systolic blood pressure						
White males	1673	5.2	5.1*	0.1	1.4*	3.8*
Black males	274	2.4	2.2*	0.2	2.0*	0.4
White females	2892	11.5	11.3*	0.2	7.7*	3.8*
Black females	667	8.6	8.6*	0.0	5.2*	3.4*
Diastolic blood pressure						
White males	1673	8.4	8.4*	0.0	3.2*	5.2*
Black males	274	1.6	1.6*	0.0	0.9*	0.7
White females	2892	13.9	13.5*	0.4	9.8*	3.7*
Black females	667	8.0	8.0*	0.0	4.8*	3.2*

* $p < 0.05$.
† Sample excludes persons with either skinfold < 5 mm.

Source: From Blair D et al, Am J Epidemiol 119(4): 526-540, 1984, with permission

Table 6
Comparison of obesity measure mean values at T1 and T2, for normotensive and hypertensive cohort studies

Obesity measure	Hypertension status at follow-up (N)	Mean (± SD)	T statistic	p value
Relative body weight (T_1)	Normotensive (176)	101.39 ± 13.21	−2.31	<0.021
	Hypertensive (137)	104.81 ± 12.72		
Relative body weight (T_2)	Normotensive (172)	104.44 ± 13.54	−3.94	<0.001
	Hypertensive (130)	111.32 ± 16.79		
Change in relative body weight	Normotensive (172)	3.04 ± 12.50	−2.45	<0.015
	Hypertensive (130)	6.97 ± 15.30		
Per cent change in relative body weight	Normotensive (172)	103.73 ± 12.61	−2.18	<0.030
	Hypertensive (130)	107.16 ± 14.69		
Quetelet Index (T_1)	Normotensive (176)	23.80 ± 3.16	−2.55	<0.011
	Hypertensive (137)	24.71 ± 3.10		
Quetelet Index (T_2)	Normotensive (172)	26.23 ± 3.35	−4.41	−0.001
	Hypertensive (130)	28.15 ± 4.20		
Change in Quetelet Index	Normotensive (172)	2.42 ± 3.27	−2.77	<0.006
	Hypertensive (130)	3.56 ± 3.86		
Per cent change in Quetelet Index	Normotensive (172)	111.20 ± 15.11	−2.15	<0.032
	Hypertensive (130)	115.10 ± 16.22		

Source: From Neser WB et al. J Chron Dis 39(2): 105-113, 1986, with permission

Table 7
Partial correlation coefficients controlling for age at T2

	Relative body weight T_1	Relative body weight T_2	Quetelet Index T_1	Quetelet Index T_2	Change in relative body weight	Change in Quetelet Index
Systolic blood pressure T_2	0.1065	0.2363	0.0962	0.2453	0.1638	0.1857
$p =$	0.065	0.001	0.96	0.001	0.004	0.001
Diastolic blood pressure T_2	0.0593	0.2618	0.0479	0.2994	0.2351	0.2866
$p =$	0.305	0.001	0.407	0.001	0.001	0.001

Source: Ibid, with permission

Table 8
Mean Systolic Blood Pressure (mmHg) by age, sex, race and study

Age (years)	NHES (1960–1962)			HANES I (1971–1975)			CHEC (1973–1975)			HANES II (1976–1980)		
	White	Black	Black – white	White	Black	Black – white	White	Black	Black – white	White	Black	Black – white
						Men						
30–39	128	137	9	126	129	3	130	134	4	125	125	0
40–49	133	136	3	130	141	11	134	140	6	128	135	7
50–59	138	153	15	138	144	6	140	147	7	136	138	2
60–69	147	151	4	141	149	8	—†	—	—	141	146	5
≥70	156	167	11	149	159	10	—	—	—	146	143	−3
Age-adjusted*	141	148	7	137	144	7	—	—	—	136	138	2
						Women						
30–39	119	129	10	119	125	6	121	128	7	118	120	5
40–49	129	142	13	126	135	9	129	138	9	123	132	9
50–59	140	158	18	136	154	18	137	148	11	134	144	10
60–69	156	169	13	148	157	9	—	—	—	141	148	7
≥70	165	169	4	153	160	7	—	—	—	148	154	6
Age-adjusted*	143	154	11	138	147	9	—	—	—	133	140	7

* Age-adjusted by the direct method of age adjustment to the HANES II population grouped into 10-year age groups.
† Dashes indicate data not available.

Source: Persky Vetal, Am J Epidemiol 124(5): 724-737, 1986, with permission

Table 9
Black/white odds ratios for prevalence of hypertension (diastolic blood pressure ≥ 95mmHg and/or drug treatment for hypertension), by age, sex and study

Age (years)	NHES (1960–1962)	HANES I (1971–1975)	HDFP (1973–1974)	CHEC (1973–1975)	HANES II (1976–1980)
			Men		
30–39	4.83	3.22	2.92	1.90	1.41
40–49	2.23	2.91	2.54	1.89	2.18
50–59	2.82	1.89	2.38	1.91	1.07
60–69	2.71	2.47	2.27	—	1.53
≥70	3.96	1.79	—†	—	1.44
Age-adjusted*					
≥30	3.22	2.50	—	—	1.52
30–59	3.41	2.68	2.59	1.90	1.54
			Women		
30–39	6.34	3.45	5.16	2.79	2.30
40–49	3.81	4.39	4.14	2.73	3.46
50–59	2.83	3.41	3.29	2.58	2.81
60–69	3.87	2.26	2.52	—	2.05
≥70	3.34	1.18	—	—	1.76
Age-adjusted*					
≥30	4.12	2.87	—	—	2.72
30–59	4.49	3.72	4.27	2.71	2.81

* Age-adjusted by the direct method of age adjustment to the HANES II population grouped into 10-year age groups.
† Dashes indicate data not available.

Table 10
Hypertension Detection and Follow-up Program: Five-year mortality by race and education Referred Care Males Ages 40 to 69 Years Entry DBP 90 to 104mmHg

Race/education	(Deaths) *N*	% Mortality	
		Crude	Age-adjusted*
WM > HS	(19) 460	4.1	4.5
WM = HS	(28) 417	6.7	7.3
WM < HS	(52) 355	14.6	12.1
BM < HS	(66) 382	17.8	16.9

*Age-adjusted by direct method. Standard population is baseline age decade distribution of all white men aged 40 to 69 years with entry DBP 90 to 104 mmHg.

Source: Reference 14
From: "Race, Education, and Five Year Mortality in HDFP Stratum I Referred Care Males. In F Gross and T Strasser (Eds) Mild Hypertension: Recent Advances, Raven, New York, 1983

Table 11
Populations in which the blood pressure increases little or not at all with age (average of both sexes, in different age groups)

Population	Systolic pressure by age group (mm Hg) 20-29	40-49	60-69	Dietary salt
Brazil (Carajas)	107	100	109	No salt: use lyes of vegetable ash (K salts)
New Guinea (Murapins)	126	126	123	0.6 gm (24-hr urine)
Botswana (Kung bushmen)	119	116	122	2.0 gm (24-hr urine)
Cook Islands (Pukapukas)	113	116	125	2.9–4.1 gm (24-hr urine)

Source: From JV Joossens. Triangle, Sandoz Journal of Medical Science, 1973, Copyright Sandoz Ltd., Basle, Switzerland, with permission.

Table 12
Populations in which blood pressure increases markedly with age (average of both sexes, in different age groups)

Population	Systolic pressure by age group (mm Hg) 20-29	40-49	60-69	Dietary salt
United States	119	130	149	± 10 gm/24 hr
Portugal	126	134	155	Not measured
Sweden	125	138	159	Not measured
Belgium	132	143	163	4–20 gm (24-hr urine)
Cook Islands (Rarontongas)	124	151	165	7.0–8.2 gm (24-hr urine)
Norway	130	141	167	Not measured
Wales	120	138	169	8.0 gm (24-hr urine)
Bahama Islands (blacks)	129	154	176	15–30 gm (24-hr urine)

Source: Ibid

Table 13
Prevalence of Hypertension for Japanese Males by Age and Geographical Location

Age	Japan	Hawaii	California	Japan	Hawaii	California
	Definite Hypertension (Prevalence/1000)			Borderline Hypertension (Prevalence/1000)		
45 - 49	139	142	234	163	222	306
50 - 54	194	183	286	203	221	280
55 - 59	255	199	263	199	252	253
60 - 64	280	247	384	239	236	292
65 - 69	318	352	423	278	288	245
Age-Adjusted Rate	223	194	315	215	235	285
No. of men	2127	7998	1795	2127	7998	1795

Source: Reference 21

Table 14
Age and Sex-adjusted Mortality Rates by Race-Ethnicity, Los Angeles County, 1980

Cause of Death	Age- and sex-adjusted* mortality rates per 100,000 population							
	Los Angeles County	White	Black	Hispanic†	Asian and Pacific Islanders			
					Japanese	Chinese	Filipino	Korean
All causes	819.9	870.2	1038.3	814.8	482.5	362.8	737.2	421.8
Major cardiovascular diseases	409.4	429.5	472.0	390.6	255.3	137.0	84.2	143.8
Diseases of heart	313.4	331.2	353.4	307.8	161.7	99.2	57.8	82.1
Total IHD	194.0	207.7	192.5	177.7	106.9	47.4	31.4	63.9
MI and other acute IHD	90.9	97.9	88.3	81.3	55.4	28.1	16.8	13.1
Chronic IHD	103.1	109.8	104.3	95.4	51.4	19.3	12.6	50.9
Hypertensive disease	21.0	19.5	47.4	--	--	--	--	--
Cerebrovascular diseases	74.3	75.8	94.2	63.5	79.6	48.7	19.7	48.3

*Direct method of adjustment with Los Angeles County population, 1980, as standard.
†Census tracts in which 75 percent or more of the population are persons of Spanish/Hispanic origin or descent.

From: "Cardiovascular Diseases in Los Angeles," Chapman, J. M. et al. Los Angeles, CA. American Heart Association, Greater Los Angeles Affiliate, Inc., 1983

Source: Reference 21

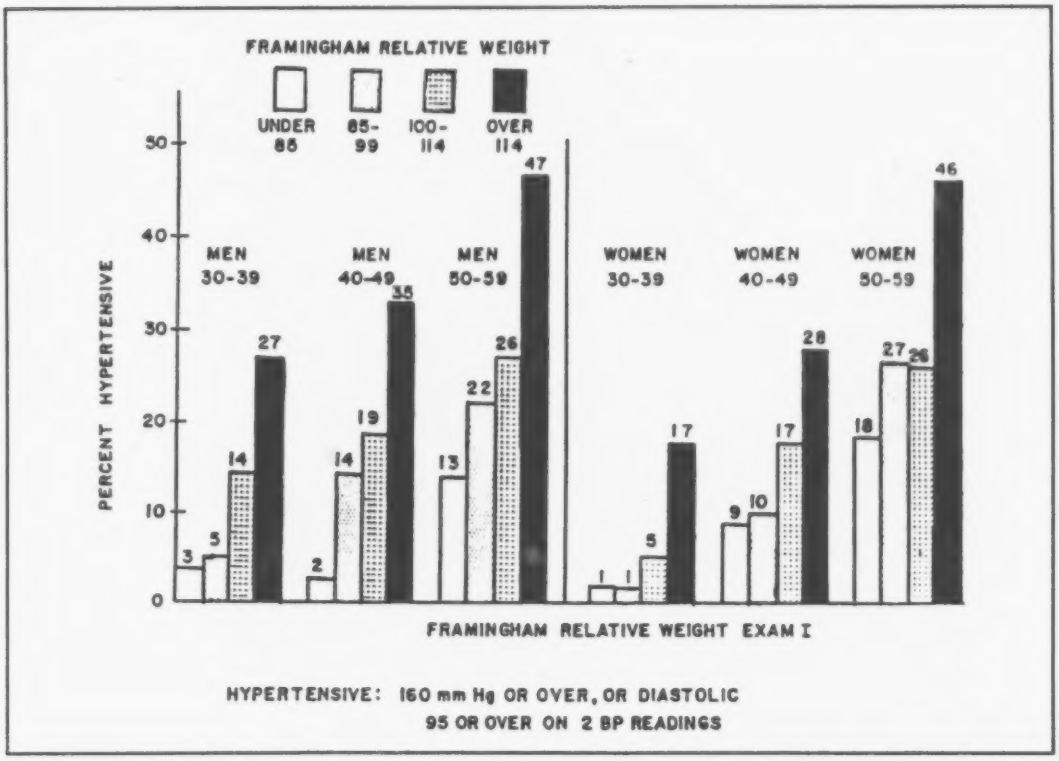

Figure 1: Prevalence of definitive hypertension by sex and age according to Framingham relative weight. Framingham Heart Study exam 1. All trends significant at 0.05 level.

Source: From WB Kannel et al, Ann Intern Med 67:48, 1967a, with permission

OBESITY AND HYPERTENSION: THE MEHARRY COHORT STUDY

William B. Neser and John Thomas
Division of Community Health Services
and Department of Medicine
Meharry Medical College
Nashville, TN

Introduction

The continued excessive hypertension morbidity and mortality among the U.S. black population demands focus upon this problem (1,2). Hypertension prevalence exceeding a rate of 40/100 has been detected in some black groups under 50 years of age, a rate two to three times that of white counterparts (3,4). While progress has been made in reducing hypertension-related mortality, hypertension control is illusive and continues to remain an unmet national health objective (5). A significant lack of progress has been noted in reduction of overweight in the population (5). Thus, the relationship between obesity and essential hypertension requires further and continued exploration.

Cross-sectional surveys of American populations reveal an association between hypertension and body weight (6-9). The association is direct in that the prevalence of hypertension increases as weight increases. The relationship between obesity and hypertension, however, has not been clear. The surveys were unable to answer whether obesity preceded or followed hypertension onset and they could not clearly place obesity in the hierarchy of hypertension precursors. Longitudinal studies specifically designed to answer these questions about hypertension precursors were initiated following World War II (8,10-14). The proportion of black subjects in these studies tended to be small or disproportionately of lower socioeconomic status. To control for the influence of such variables as education and occupation, Dr. John Thomas of Meharry Medical College began a study of black medical students parallel to the one on white medical students initiated by Dr. Caroline Thomas at Johns Hopkins (15-16). The results reported here represent a second phase or follow-up of the Meharry Cohort Study.

The relationship of obesity to hypertension has been viewed as important for several reasons: 1) In view of the direct association between the two, obesity has been cited as a major risk factor in hypertension etiology. 2) As an obvious risk factor, obesity has been used as a marker for potential case identification. This risk factor is highly prevalent as 30 percent of black males and 49 percent of black females are obese (3). 3) The use of weight reduction as a possible non-pharmacological intervention for obese hypertensives has been explored and advocated (17). In all of these aspects there has been an element of uncertainty. The role and relative importance of obesity in hypertension etiology and treatment, particularly for the black population, remains poorly defined (18).

Reviews of the literature suggest that the obesity-hypertension relationship is not consistent for the black male (6,19,20). Cross-sectional studies suggest that some black males form an exception to the association between obesity and hypertension (8,9,21). Longitudinal studies confirm this finding (8,11,22). The purpose of this paper is to reevaluate the position of obesity in black male hypertension.

Methods

The data reported here were obtained from initial and subsequent examinations of 341 or 78 percent of the total 433 black male cohort. Initial examinations were made between 1957 and 1965 (T_1) while these men were medical students. Students admitted to the study were hypertension free (systolic<140 mmHg, diastolic<90 mmHg) and were free of other significant medical conditions (15). Subsequent follow-up examinations were conducted upon these physicians between 1981 and 1983 (T_2), a mean time of 22.5 years after the first examination.

The same examination procedures were followed at T_1 and T_2. Weight was reported to the nearest half pound and was obtained on a standard scale with shoes and outer clothing removed. Height was measured to the nearest half inch. Body mass was measured by weight/height^2 (Quetelet Index). Relative body weight (RVW) was obtained through comparing individual height and weight with the 1959 Build and Blood Pressure Tables (23). Casual, supine blood pressure measurements were obtained following standard techniques (24). Hypertension was defined as blood pressure greater than 140/90 mmHg or physician prescribed antihypertensive regime, or interim history of hypertension.

Results

Hypertension

As reported elsewhere, a remarkable 43.85 percent of the cohort were found to have developed hypertension between T_1 and T_2 (22,25). This prevalence was found in the 341 reexamined physicians. Of these 131 hypertensive physicians, 39 had systolic pressure exceeding 160 mmHg and 36 had diastolic pressures in excess of 110 mmHg. A history of hypertension was presented by 77 (58.8 percent) physicians. In 44 (33.6 percent) physicians the hypertension was first detected by the research team. The Meharry Cohort hypertension prevalence corresponded reasonably well with that for the same age, sex and race found in a national survey (26).

Obesity

Relative Body Weight

As anticipated, the T_2 data resembled recent surveys in that there was an association between weight and blood pressure. Figure 1 illustrates the increased risk of hypertension with increased relative body weight. As relative body weight increased from less than 110 percent to 130 percent, or greater, percent of hypertensive males increased from 36 percent to 63 percent. This result provides a risk ratio of 1.75 times more for hypertension in the most obese group compared with the leanest groups. As Table 1 indicates, using an obesity level of greater than 120 percent relative body weight, weight status at T_1 did not predict hypertension status at T_2, ($p>0.80$). At T_2, however, the obesity-hypertension relationship was present and statistically significant ($P<0.03$).

The relative body weight of black physicians at T_1 was compared with hypertension status and relative body weight at T_2. A total of 40.2 percent of those who were not obese at either time became hypertensive. Likewise, only 36.4 percent of those who had lost their obesity between the two measurement times became hypertensive. For the physicians who remained obese, the amount of hypertension was 45.5 percent. The group most at risk for hypertension were those who became obese during the study period. The age adjusted relative risk of those who became obese compared to those who remained lean was 1.48. The percentage of hypertension among those with acquired obesity was 59.1 percent.

Quetelet Index

When the Quetelet Index was used, there was an association between T_1 obesity status and T_2 blood pressure but not in the expected direction. Those in the middle category of > 27 but < 29.3 kg/m^2 had the highest percentage of hypertension. (See Table 2). At T_2, however the gradient of hypertension risk increased as the Quetelet Index increased and the association was statistically significant.

Mean obesity values for the Quetelet Index and Relative Body Weight were compared by hypertension status at T_2, obesity values at T_2, change in obesity values T_1 - T_2, and percent change T_1 - T_2, all indicated statistically significant differences between hypertensive and normotensive subjects. Nearly identical results were obtained using either mean Relative Body Weight or mean

Quetelet Index. Partial correlations adjusting for age at T_2 eliminated the T_1 association between obesity and T_2 blood pressure for both obesity measures but the statistical significance remained for T_2 obesity and T_1 - T_2 changes in obesity. Also, when physicians receiving medication were omitted, the age controlled correlations remained essentially the same. No medication effect could be seen in the obesity-blood pressure relationship.

Social and Biomedical Variables

Obesity together with other social and biomedical variables were examined in a regression of follow-up blood pressures. (See Table 3). Using either Quetelet Index or Relative Body Weight as an obesity measure, change in obesity measure had the highest F ratio of all the variables tested. Other statistically significant associations for both T_2 diastolic and systolic blood pressures were baseline diastolic blood pressure, smoking and length of time in study. Omission of physicians receiving medication did not alter the significance or relative F ratio positions of the variables studied.

A statistical model was constructed to differentiate between normotensive and hypertensive men. Table 4 illustrates that the discriminate function scores of T_1 diastolic blood pressure, length of time in study and change in Quetelet Index contributed the highest F statistic values. Smoking, positive parental history for stroke or hypertension, and baseline weight and age also were statistically significant. A total of 69 percent of the variance in discriminating between normotensive and hypertensive subjects is accounted for by this model. Again, the same results were obtained by using Relative Body Weight as the obesity measure. Neither T_1 serum cholesterol nor heart rate assisted in the discrimination between hypertensive and normotensive physicians.

Discussion

These results form a puzzle. The contribution of obesity to discrimination of hypertensive from normal subjects is very persistent. It appears significantly in all the statistical analyses we performed. Yet, while 56 percent of the obese black males in this study were hypertensive, only 24 percent of those with hypertension were obese. In our previous work we had shown that the addition of certain risk factors, including obesity, multiplied the risk for hypertension (22,25). Does the presence of obesity, particularly acquired obesity, merely multiply the chance of hypertension or are we dealing with two syndromes? A subgroup of the Third International Conference on Obesity suggested that obesity might lead to essential hypertension through metabolic derangement (27). In particular, sodium retention from hyperinsulinemia and related disorders of obesity may contribute to hypertension. It has also been suggested that decreased glucose tolerance and elevated plasma triglycerides, resulting from obesity, contribute to the onset of hypertension (28). Thus, there is an already existing suggestion that obesity forms a separate syndrome or sub-family of hypertension. Unfortunately our data are not in a form to provide more definitive answers about the possibility of an obesity-hypertension syndrome in black males. Regardless of how it is viewed, obesity is a significant risk factor in the hypertension of many blacks. Weight reduction holds the potential for being an important non-pharmacological treatment modality.

The Meharry Cohort Study is unique. It consists of middle class male, black physicians who were initially studied while they were healthy medical students. Some of the study limitations regarding sample size and representativeness have been reported (15,16,22,25). Selectivity against obese medical students may have existed. If so, the bias would have emphasized the role of acquired obesity rather than static obesity in hypertension. However, obesity and hypertension results parallel those obtained in the same age, race and educational level by the Hypertension Detention and Follow-up Program and tend to negate the possibility of a overall bias against obesity (4). Of more concern is the lack of interim weight measures between T_1 and T_2. It is possible that weight may have been gained and lost by the black physicians before the T_2 measurements and individual subjects wrongly classified as "lean" or "obese" on the basis of their T_2 measurements. The results, however, are consistent with other longitudinal studies (8,11).

Measurement has been another source of concern in this study. There has been much discussion in the literature regarding the choice of

measurements to reflect obesity as body fat rather than just excess weight (12,14,29-31). The Quetelet Index used here has been recommended for ease of application (31). As confirmed by the results of this study, the relationship between obesity and hypertension exists regardless of which measurement is employed (14).

Obesity was found to be an important risk factor but only in a limited number of instances in this study. The durability of long term weight management, too, would appear to be rather limited at this point (32-34). For the lean 76 percent of hypertensive men found in this cohort, hypertension management will have to depend upon other modalities. Thus, the relationship between obesity and hypertension etiology and management remains significant but of limited importance.

However there is no doubt that weight reduction reduces hypertension and enhances the therapy of other, additional regimes.

Acknowledgement

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TABLE 1. DISTRIBUTION OF COHORT SUBJECTS BY WEIGHT STATUS AT INITIAL EXAM (T_1) OR FOLLOW-UP EXAM (T_2), AND BY HYPERTENSION STATUS ON FOLLOW-UP EXAM (T_2)

	Hypertension status T_2		
Weight status at T_1	Normotensive	Hypertensive	Total
Not obese (≤120% relative body weight)	163 (56.4%)	126 (43.6%)	289
Obese (>120% relative body weight)	13 (54.2%)	11 (45.8%)	24
Total	176	137	313
Chi square = 0.045, $df = 1$, $p > 0.80$			
	Hypertension status at T_2		
Weight status at T_2	Normotensive	Hypertensive	Total
Not obese (≤120% relative body weight)	148 (59.9%)	99 (40.1%)	247
Obese (>120% relative body weight)	24 (43.6%)	31 (56.4%)	55
Total	172	130	302
Chi square = 4.22, $df = 1$, $p < 0.03$			
Adjusted* RR = 1.43 (1.05, 1.94)			

*Adjustment is for age at entrance into the study.
Mantel-Haenszel chi square = 5.14, $p < 0.03$.

TABLE 2
DISTRIBUTION OF COHORT SUBJECTS BY QUETELET INDEX OF WEIGHT AT T_1 AND AT T_2, AND BY BLOOD PRESSURE STATUS AT T_2

Quetelet Index T_1 (kg/M^2)	Blood pressure status (T_2)		Ratio risk	Total
	Normotensive	Hypertensive		
27 or less	152 (58.7%)	107 (41.3%)	1.00	259
> 27 to < 29.3	13 (37.1%)	22 (62.9%)	1.52	35
29.3 and above	11 (57.9%)	8 (42.1%)	1.02	19
Total	176	137		313
Chi square = 5.838, $df = 2$, $p = 0.054$				
Quetelet Index T_2 (kg/M^2)	Blood pressure status (T_2)		Ratio risk	Total
	Normotensive	Hypertensive		
27 or less	111 (66.1%)	57 (33.9%)	1.00	168
> 27 to < 29.3	30 (50.9%]	29 (49.1%)	1.45	59
29.3 and above	31 (41.3%)	44 (58.7%)	1.73	75
Total	172	130		302
Chi square = 14.06, $df = 2$, $p < 0.002$				

TABLE 3

SUMMARY OF REGRESSION OF FOLLOW-UP BLOOD PRESSURES ON QUETELET INDEX AND OTHER CHARACTERISTICS

Independent variables	Follow-up SBP		Follow-up DBP	
	Regression coefficient: B	*F*-ratio	Regression coefficient: B	*F*-ratio
Baseline SBP	0.473	10.676*	0.087	0.982
Baseline DBP	0.485	8.793***	0.436	19.411***
Change in Quetelet Index	1.219	12.720***	1.026	24.597***
Smoking	3.577	5.600*	1.796	3.851*
Length of time to follow-up	1.587	7.832**	1.117	10.585**
Age at baseline	0.727	4.712*	−0.173	0.729
Baseline Quetelet Index	0.551	1.695	0.580	5.122*
Baseline heart rate	−0.151	1.364	0.109	1.951
Parental history of hypertension or stroke	1.083	0.765	1.137	2.302
Baseline cholesterol	0.007	0.098	−0.002	0.013
Constant	(−26.00)		(−5.50)	
R^2	21.76%		26.76%	
Model *F* statistic (10,241)	6.704		8.803	

.*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

TABLE 4

Obesity and Hypertension in Black Physicians 111

GROUP MEANS, DISCRIMINANT FUNCTION SCORES AND *F* STATISTICS FOR NORMOTENSIVE AND HYPERTENSIVE SUBJECTS

Variable	Group means		Unstandardized discriminant function coefficient	*F* statistic	Significance level
	Normotensive	Hypertensive			
Baseline DBP	72.14 ± 7.52	76.65 ± 7.38	−0.05472	22.716	$p < 0.001$
Length of time to follow-up	21.85 ± 2.17	22.58 ± 1.92	−0.17838	10.668	$p < 0.005$
Change in Quetelet Index	2.35 ± 3.19	2.65 ± 3.85	−0.12937	8.033	$p < 0.005$
Smoking	0.96 ± 0.77	1.15 ± 0.78	−0.36443	7.924	$p < 0.01$
Parental history of hypertension or stroke	0.54 ± 0.80	0.95 ± 1.07	−0.32864	6.508	$p < 0.025$
Baseline Quetelet Index	23.76 ± 3.17	24.44 ± 2.73	−0.07641	6.930	$p < 0.025$
Baseline SBP	116.95 ± 9.46	121.41 ± 8.00	−0.03006	3.522	$p < 0.10$
Age at baseline	27.28 ± 3.73	27.95 ± 3.70	−0.05464	2.619	$p < 0.025$
Constant			15.91952		

Serum cholesterol and baseline heart rate had *F* levels insufficient for inclusion in the model.
Overall *F* statistic (8,243) = 9.261, $p < 0.001$.
Rao's $V = 76.22$, $\chi^2 = 66.24$, $df = 8$, $p < 0.001$.

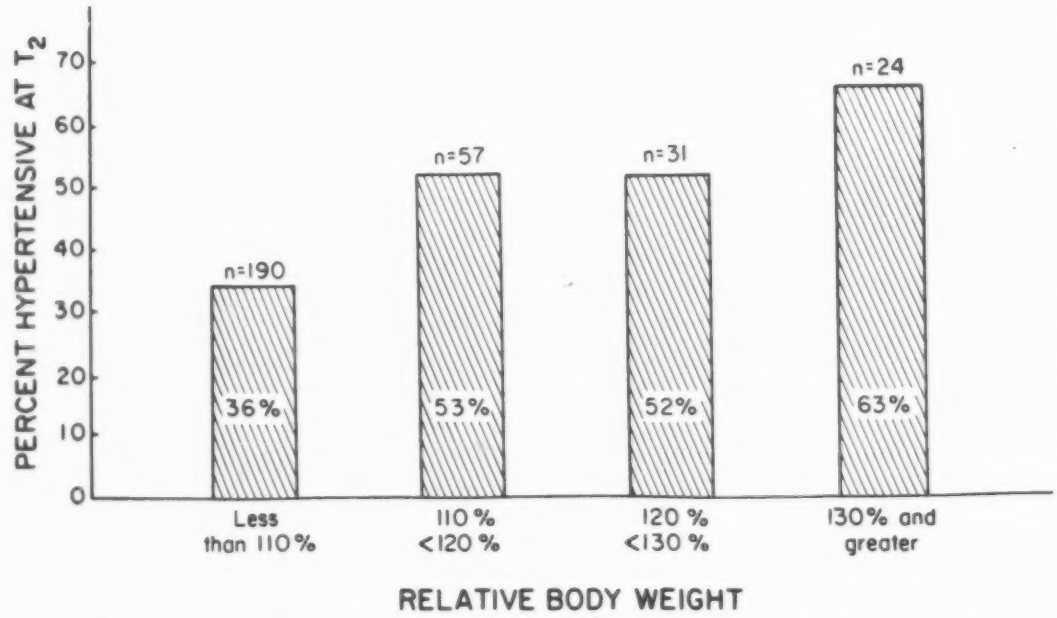

Figure 1. Distribution of cohort subjects by relative body weight and hypertensive status at follow-up.

Fourth Scientific Session - Discussion

Dr. Grossman:
Was there a significant number of female physicians to make any contribution to this analysis?

Dr. Neser:
No, that was why we ruled them out. There were 38 all together, and we really did not have enough to make a difference compared to the 300 plus males that we surveyed.

Dr. Falk:
Stress is a thing that you have studied for decades in connection with this group. What do you have to say about its relationship either to the study or just to the subject?

Dr. Neser:
We did not study stress separately in this group. We considered that all physicians were under some stress. When we did a type A study, we found that type A was not related to hypertension, type A varied by kinds of practice - surgeons were super type A; psychiatrists were laid back and a great majority of them were type B. But if you use Type A, Type B as a measurement it did not relate. I would assume that we need finer instruments for stress, and Fred may be, could answer that better than I.

Dr. Kumanyika:
Your observation that there is more non-obesity related hypertension in blacks confirms what has been seen in, I guess, Evans County and several cross-sectional studies. Do you have any information to the effect that this is more severe hypertension as Barret Connor (?) has suggested in these black men who are not obese?

Dr. Neser:
I will defer to John, John my coauthor, do you have any
feeling on that?

Dr. Thomas:
No, there wasn't any difference in the level of hypertension. It seemed that the leaner male had more.

Dr. Kumanyika:
As a component of obesity research, I really think that looking into lean hypertension is more important for the black population than of obesity related hypertension.

Dr. Howard:
There is a lot of interest at the moment in the fact that the distribution of the fat mass importantly impacts on whether or not there is associated mobidity, and do we have any data from this study about whether or not the cohorts at the beginning who were apparently nonobese but not associated with hypertension, later on acquired obesity was this a different type of obesity that these people acquired?

Dr. Neser:
Not that I know of, Dr. Thomas, do you know of any.

Dr. Thomas:
No, we did not have any.

Dr. Howard:
You did not do any thigh, waist measurements?

Dr. Neser:
No, we did not do any.

Dr. Grim:
Dr. Neser, since you now can predict possibly if your graduates are going to develop hypertension, what educational activities are you taking on your current students to do something about high blood pressure and diet and possible preventive aspects? We don't know how to prevent it yet, but what are you teaching them now, so that they won't get it twenty years from now?

Dr. Neser:
Each student that goes through the community health rotation gets a health risk appraisal and is personally evaluated and introduced in a sense to the risk factors that are present. Dr. Thomas also sees these students in the cardiology rotation and I am sure that he can speak for himself on that.

Dr. Thomas:
Well we teach them about risk factors, but I am not sure how effective it is. The treatment of the black physician - there needs to be some type of intervention. We found that out of all of the black physicians who have hypertension, only 10% of them have been seen by another physician to control their blood pressure and others were taking medicine, but if they had side effects they would stop taking it, and so we propose with the association of black cardiologists to form a hypertension registry where individuals can register, and actually we have done some control with physicians in Mississippi.

Dr. Grim:
It is not unique to black physicians, I don't think.

Dr. Grossman:
I may have missed the point, but are you making the point that the incidence of hypertension among black physicians is greater than the incidence of hypertension in the black population at large?

Dr. Neser:
It is the same.

Dr. Grossman:
That was what I thought. You said about 40%?

Dr. Neser:
Fourty four percent, it is the same. That's why we are saying we don't think there were biases real great as to who got into this cohort, because given the age, education level that the hypertension detection study found, we found the same rates.

Mr. Scott:
Dr. Iacono, during your intervention period, when you switched to the low fat diet, did you see any differences in the lipoprotein composition?

Dr. Iacono:
Yes we did and there were changes in certain of the apoproteins we looked at. However I can't remember precisely what they were, but they were there. I can refer you to a reference for that. But there were very dramatic changes which we got, as you saw in the LDL and the HDL and these were in a ratio of one. We always got the decline; we got a decline ranging from 12 to 23% of cholesterol in every intervention study we have conducted.

Mr. Scott:
We saw the drop in the blood pressure. Was the drop greater in the individuals that were at the higher end, in terms of the higher end of the cholesterol levels than they were in individuals that were at the lower end of the cholesterol levels initially?

Dr. Iacono:
That would tend to be the case, but we could not predict.

Dr. Rogel:

My question is for Dr. Iacono. What I am concerned about is that any type of change in the lipid, in the polyunsaturated fat content would primiarily be with linoleic acid - is that correct? The reason I am asking is that if you look at very primitive diets, for example, there have been some studies with diets of the Aborigines in Australia, and they look at the actual fat content of the animals - kangaroos or whatever animals they are looking at - they are very low in triglyceride fat, most of the fat that is contained in those animals would be phospholipid membrane fat, which would be very high in arachidonic acid and perhaps also in some omega - 3 - fatty acids.

We know that in humans and mammals, that the conversion between linoleic acid and arachidonic acid is really not all that terribly efficient, or at least it seems that way from some of the studies that have been done. So, would you like to comment in view of the fact that people on more primitive diets would tend to have less hypertension - that there may be some relevance to the type of fat that they are getting, as well as between the quantity of fat?

Dr. Iacono:

That's a very interesting question, and that question in fact came up in Australia in a meeting which I attended. Precisely almost the same question which you are posing.

To begin with, it is very difficult to predict. Obviously those animals that were eaten in primitive times were far leaner and did contain more polyunsaturated fats. Perhaps the big difference would be that they were eating less saturated fats because the animals, being leaner, did not have as much fat pad on them, and so the people were eating the membrane fatty acids in terms of the fat more so than the deposited fat. But from the point of view of just how this might have affected blood preessure, I think one can only speculate. I would guess that, yes, you would have a lower blood pressure assuming that our data are real in terms of the reduction of blood pressure by linoleic acid - that is, the N6 fatty acid that we are talking about. But one can only speculate about that, I am sure, because there are other complicating factors in that diet. If you are a hunter/gatherer and if you are in the period when you are eating mainly meat from animals that you are hunting, your protein intake becomes extremely high, and so the associated health problems dealing with very high protein diets become paramount and so it supercedes any effects that you may have relative to high fat diet. This is well known. We know that in animals, for example, that if you eat a diet very high in protein, that is 35-40%, the animals don't live very long, they just die from some form of kidney diease, usually nephrosis.

Dr. Carter:

The linoleic to DGLA to arachidonic acid is not the only pathway, and that pathway is dependant on the delta desaturate enzyme. You can go from linoleic acid to DGLA to prostaglandic E1, which is a vasodilator, and that may be one of the mechanisms by which there is this lowering of blood pressure and a lowering of levels of cholesterol, because the GLA may be converted into some other prostaglandin metabolite which is effective in lowering total cholesterol.

The question I have for Dr. Iacono is that the other side of that equation, on the other side of the prostaglandin E2 series, you have Omega 3 fatty acids. Have you done some studies where you have increased the amount of Omega 3 fatty acids, either coming from fish oil or coming from plant oils, like linseed or flaxseed?

Dr. Iacono:

Yes, well I must say to you, "no", we have personally not done experiments with the Omega 3 fatty acids; we are about to embark on one in early January where we will try to look at the nutritional effect of Omega 3 fatty acids, but superimposed on the N6 fatty acids. However there have been experiments conducted, as you know, on Omega 3 fatty acids, albeit not well nutritionally controlled, and again this is the bias which each of us investigators have, and taking in large amounts of N3 fatty acids, as you know, appears to have some effect upon blood pressure, and it is thought to occur through perhaps specific inhibition of certain enzymes of the 2-type prostaglandins. But you have to take in large amounts of the fish oil, and so the question is, you are out of the nutritional phase and into pharmacology.

Now, with respect to this other point, which may shed some light on your question of the gammalinolenic acid, there have been some reports now that these types of oils (there are two types - borage oil now has been used, and evening primrose oil has been used) which lead to PGE1 formation and which appear to also lower blood pressure. Now, the degree to which this occurs is somewhat unknown in man, because man does not eat this kind of oil, but there is experimental nutrition research going on in this area now, and perhaps in a few years we will know more about this.

Dr. Edozien:

I wish to compliment the presenters this afternoon because they showed some very excellent data, but there are some questions that I would like them to comment on. Now, the first comment I would like to make is, from population studies of blood pressure, I think it becomes very clear that the major factors involved are age, sex, race, dietary fats and body fats. Now, we are running around the world trying to do these studies. When you go to anywhere in Africa, you will have there people who have the widest range of fat intakes, from less than 10% to half fats, wide range of body fats, and all the factors are there. Many of the questions we are discussing, like many other issues, can best be resolved if some of this research can be done in those parts of the world. Now, fortunately, like most things, here we have money, the resources and the manpower, but unfortunately over there we have the materials but no money for research. And the question is, how can the two meet. I hope that one of the things we accomplish from this conference is to think about these things, because it is very difficult to get financial support to do overseas research. Many of the issues we are discussing now can best be resolved by working overseas, and I want to make that point.

The second point I would like to make is in connection with Dr. Iacono's paper and the question of dietary fats and blood pressure. One of the things that was not mentioned is that nature has a way of balancing a lot of things so as to make things remain on an even keel, and when you alter dietary fats you alter carbohydrates. Carbohydrates also reduce blood pressure, so when you increase fats and lower carbohydrates, you reduce the blood pressure by increasing fats, but you increase the blood pressure by reducing carbohydrates, so on balance the change is minimal, and I think the effect of carbohydrates should not be forgotten in these kinds of studies, because it is a very, very important factor.

Finally, in dealing with the question of mechanism, as I described the other day, we have done experiments, also population studies and experimental studies in the rats, and it is clear that dietary fat does have tremendous effect on the endocrine system, all leading to the reduction of blood pressure. And, in studying the rat, we also got changes in prostaglandins and changes in ACTH and the adenocortical system. It turns out, at least in our study, that changes in cholesterol are very closely related to changes in prostaglandins, but changes in blood pressure are more clearly related to changes in ACTH and the adenocortical system. I think that is something that you might consider when you consider the work dealing with the mechanism by which it occurs. And changes in ACTH are related also to excretion of calcium, the excretion of sodium, and retention of potassium - they all go hand in hand.

Dr. Howard:

Does any of the panel want to respond to all of that? Any more questions before we close this afternoon?

Dr. Grossman:

I have one more question for Harvey Anderson. Harvey, the classic case of dietary acute hypertension in the patient on MAO inhibitors who eats tyramine containing foods, are there any other examples of tyramine rich diet promoting or causing or contributing to hypertension, or does it have to be just that special situation?

Dr. Anderson:

As far as I know, it has to be that special situation in order to bring about acute hypertensive episode, but I think that the problem with a lot of the studies in examining protein and protein foods still is that there is a false negative built into the way the studies have been done, because

I think that again, if Jack were to apply the same kind of change in food components but not the food per se, with a manipulation of protein content, so that fat and carbohydrate stayed the same, I think I would believe that we have an answer to the question, but the way that so many of the studies have been done in terms of modifying foods leads to other changes - well, changes so many components, including the foods in which these false neurotransmitters are present. Now, they by themselves can't or may not change unless you do have the MAO inhibitors, but I'm just not convinced that, given the mechanistic effects, at least that occur in rats, I can't believe that these don't under some circumstances apply in the human, and we haven't looked at it. If you look at again changing dietary fats, certainly in the rat, and we get back to the points about mechanisms - dietary fat composition does in fact change rat neuromembrane composition and changes the functionality of the transport mechanisms in the central nervous system. That is pretty recent work. But certainly, even within four to six weeks of giving the rat a change in diet, polyunsaturated vs. saturated, you will change phospholipid neural cell membrane composition. You can show that analytically and you can also show transport and functionality of those neurons changing, and you can show animal behavior changes. So I think once you start manipulating the fat, some of the central mechanisms that I was trying to allude to also change. I guess my question of Jack is when do you think that the composition of fat becomes important in the context of quantity of fat, and I agree with Dr. Edozien that carbohydrates per se in terms of mechanisms are important, but just when do you think that composition becomes important within the construct of amount?

Dr. Iacono:

Well, I think composition become extremely important when we are talking about the optimal function of the kidney. If the kind of information that is coming through now, which is going to appear in the literature very soon, by Dr. Carlos Romeros at Rochester, in which he is showing by some elegant experimentation that the prostaglandin levels in the kidney are directly related to the renin-angiotensin system, and that as you increase the levels of certain of the prostaglandins, you increase, well, for example, he states very clearly that as you increase the prostacycline of the kidney, you increase the production of renin in kidney, which in turn stimulates the formation of prostaglandin E2, which in turn affects angiotensin 2 formation. It seems like this series of reactions, of interactions, of prostaglandins with the renin-angiotensin system, is real in kidney. If this is the case, then the question is how much linoleic acid do we have to eat in order to stimulate the production of optimal levels of these prostaglandins in kidney? This has always been a mystery to us. We know that we are raising the linoleic acid content of the diet from 3-4% of calories up to 5-10% of calories. This is a huge dose of linoleic acid, but in order to get an effect on blood pressure, you have to wait about 4-6 weeks. Now, it certainly is not that there is a shortage of arachidonic acid in tissue membranes, because if you look at any tissue membranes in the body, there is a trememdous amount of arachidonic acid. There is no shortage of arachidonic acid if you look at the phospholipid species of tissue, particularly of kidney. Yet, in order to influence blood pressure, you have got to feed the linoleic acid, as I say, for a certain period of time. Now, what happens to these levels of prostaglandins in kidney and at the level of endothelial cell? They appear to go up in animals. I shouldn't say they appear to go up - they go up in rat experimentation - that is very clearly defined. We don't have data in man, so the quality of the fat, in answer to your question, which is a sort of roundabout way to get to the answer, the quality of the fat has to change also. And we think that we are improving the nutritional status of the kidney, and by improving the nutritional status of the kidney, we improve the excretion of water and salts. Now, we showed one experiment here where the volume of urine was shown to be increased under a polyunsaturated fatty acid diet. We have three models now to show this - three separate experiments which we have conducted where we show this effect, and we have a whole lot of data now where we are looking at the excretion of minerals - sodium, potassium, calcium, phosphorus, magnesium and zinc. And I might say to you, there are some very

exciting changes that we are observing in the excretion of these minerals. I might say that we are also controlling the intake of these minerals and these data will be coming forth shortly. But definitely you have to change the quality of the fat as you reduce the fat.

Dr. Thomas:
In addition to all of the metabolic changes with weight reduction, there is a lot of blood vessel function that go with that. Do you think that decreasing peripheral resistance by weight loss plays any part in reducing the blood pressure?

Dr. Iacono:
Well, that is the $64,000 question. I wish we could answer that. I would say that whatever might happen physiologically that would improve peripheral resistance would inevitably improve blood pressure. Now, how this occurs during weight loss, I don't know the answer to that, Dr. Thomas.

Dr. Howard:
Can I just sort of finish off here? I think one of the most important take-home messages that I personally want to get back to Albany with is a very clear summary of the fact that you said that from the long cohort study at Meharry, you can predict 70% which black male is going to become hypertensive. If you have to give in order those factors which are going to most heavily bear on that prediction and outcome, would you just make sure that we have heard them, so that we go home with them ringing in our ears?

Dr. Neser:
I hate to put them in order, because as we analyze them differently, we come up with a little different pecking order.

Dr. Howard:
Try.

Dr. Neser:
Primarily, family history, positive family history of stroke or hypertension, it is a risk factor that clinicians should look for, and Dr. Thomas has a paper that is coming out on that soon.
Secondly, certainly, early high-normal diastolic and systolic pressure. In other words, a teenager who has pressures that are near the borderline.
Attained obesity, I would put in there, and then the other, more traditional ones, of age and smoking, I would rate.
Cholesterol in the younger adult did not predict at all. I want to emphasize that, because we have been talking about cholesterol. It didn't work in our studies.

Dr. Howard:
That was helpful. Thank you. Thank you, everybody.

Fifth Scientific Session

Chair *Wallace T. Williams, Ph.D, R.D.*

CHILDHOOD ANTECEDENTS OF HYPERTENSION IN ADULT LIFE

Bruce S. Alpert
Division of Cardiology and
Department of Pediatrics
University of Tennessee, Memphis

The precursors of essential hypertension (EH) have their origins in childhood. The morbidity and mortality which occur directly and indirectly from EH represent a major portion of the health care costs in the United States. It is well known that Blacks and descendents of parents with EH have a higher incidence of EH than do the remainder of the population. We and others are seeking to identify markers for later-onset hypertension in high risk children which could lead to the primary prevention of EH in adult life. Therapy for EH is expensive and frequently leads to an unacceptable change in the patient's lifestyle. The primary prevention of EH, rather than the therapy of already established EH should be the goal of a significant portion of the health care research in the United States.

It is estimated that almost 58 million Americans either have EH or take antihypertensive medications. The prevalence of EH is higher in Blacks (38%) than in Whites (29%) [1]. One of the major goals of the Departments of Agriculture and Health and Human Services, as well as the American Heart Association and the American Academy of Pediatrics, has been the recommendation of dietary guidelines which will lead to a reduced incidence and prevalence of cardiovascular disease, and in particular, EH [3-6].

There are few data which are known concerning the nutritional intake, in particular minerals, of children. For this symposium, I will restrict my topic to what is known concerning sodium intake and the evolution of EH. A study by Hofman, Hazelbrock, and Valkenburg [7] showed that a reduction in the sodium intake in infants studied during the first six months of life was associated with lower systolic blood pressure. The sodium intake of the low-sodium group (0.89 ± 0.26 mole) was about one-third of that of the normal-sodium group (2.50 ± 0.95 mole). The growth of the infants in the two groups was equivalent until the 21st week of life, when the babies in the low-sodium became heavier than the babies in the normal-sodium group. By the end of the 25th week, systolic blood pressure was a mean of 2.1 mmHg higher in the normal-sodium group. The authors concluded that their data were consistent with the view that sodium intake is causally related to blood pressure level. This study highlights the importance of the concept that prevention strategies, to be maximally effective, need to be started as early in life as possible.

The dietary statement of the American Academy of Pediatrics in 1974 [4] stresses many of the problems with our societal intake of sodium. In past years the sodium content of infant formula and food was determined by the need to satisfy the mother's salt appetite. Infants have no preference for food with either low or high salt content [8]. Beginning in the early 1970's, the infant food industry began to respond to the scientific findings and initiated reductions in sodium content of formula and foods.

The determination of safe levels of sodium intake for human infants and children has also been addressed by the National Research Council [9]. The minimal sodium requirement of infants and children exceeds that of the adult, primarily related to growth. Each kilogram of increase in body weight requires 90 mEq of sodium. Adults do not require sodium for growth. The healthy adult excretes approximately 1 mEq/day in each urine and fecal loss. Another 2-4 mEq of sodium is required to replace insensible loss through the skin and

lungs. The total adult sodium requirement to maintain sodium homeostasis is 4-6 mEq/day. In the United States, adult daily sodium intakes vary between approximately 100-300 mEq [9]. Thus, assuming an average need of 5 mEq/day, adult Americans are consuming from 20-60 times the required sodium intake to insure physiologic needs. The initiation of moderate to severe reductions in sodium intake could not be expected to result in the reduction of sodium to a level which could be physiologically dangerous.

The sodium needs of the infant exceed those of the adult [9]. The infant requires from 1 to 2 mEq/day for growth. Skin and gastrointestinal losses have been reported to be another 2 mEq/day. Urinary losses are approximately 3-4 mEq/day. Thus, the infant requires at least 6-8 mEq/day of sodium for proper growth and development. The composition of the milk fed to the infant is a critical variable in the total amount of sodium consumed in the first year of life. Human milk contains an average of 7 mEg/L. Commercial formulas contain sodium in a concentration which ranges from 7 to 17 mEq/L. Cow's milk contains 21 mEq/L of sodium. Thus, breast feeding or choosing a formula low in sodium will result in a substantial reduction in the infant's sodium intake.

The National Research Council's Recommended Dailey Allowance (RDA) gives a range of "safe" levels of sodium intake for the infant, child, and adolescent, based upon age. These values are tabulated below [9]:

	Na Intake	
Age (Yr)	Mg	mEq
0 - 0.5	115 - 350	5.0-15.2
0.5 -1	250 - 750	10.9 - 32.6
1 -3	325 - 975	14.1 - 42.4
4 -6	450 - 1350	19.6 - 58.7
7 - 10	600 - 1800	26.1 - 78.3
11+	900 - 2700	39.1 - 117.4

The scientific bases for these recommendations are from population observations, rather than physiologic calculations. In each case, the upper limit of sodium intake is three times the lowest intake recommended. The RDA states that consumption of "human milk, infant formulas, and unsalted infant foods appears to be both adequate and safe for the young infant" [9].

Data of actual sodium intake of children in the Southern United States are scarce. The Bogalusa Heart Study has been the most productive in that regard [10,11]. The sodium intake of a free-living population of healthy students from 8-18 years of age was 2,729 mg (118.7 mEq) prior to intervention, and 2,921 mg (127 mEq) post-intervention. In comparison to the RDA recommendations for these ages (see table above), these children's mean values exceeded the upper limit of safety by a substantial margin.

Older data from a Department of Agriculture survey summarized in the 1974 American Academy of Pediatrics Statement [4] indicate that infant intake of sodium is similarly excessive. For example, the RDA gives the upper limit of safe intake at 6 months of 15.2 mEq, and 12 months 32.6 mEq. Again, the mean values of sodium intake discovered were 29.0 mEq and 63 mEq, respectively. In each case, the mean value exceeded the maximal recommended value by a factor of 2.

The task of succeeding in the reduction of sodium intake to aid in the prevention of adult-onset EH is overwhelming. The basic question to be answered is whether only high risk individuals need to be treated, or whether the intervention on the population at large would be the most beneficial from the stand-point of epidemiology and public health. There are adequate data which show that only a minority of the population is 'salt sensitive' [12], indicating that increased sodium intake leads to higher blood pressure, and reduced sodium intake produces lower blood pressure.

Investigations on our campus, UT, Memphis, (Jay Sullivan, M.D., personal communication) and by others [12-14] have shown that about 15% of healthy White adult volunteers and approximately 30% of Black adult volunteers are salt-sensitive. A preliminary study by our group suggests that the prevalence of salt-sensitivity in Black adolescents may be higher than 30%. "There is a reasonable possibility that a low salt intake begun early in life may protect, to some extent, persons at risk from developing hypertension" [4]. The problem for the public health official is to identify these individuals. The determination of salt sensitivity requires rigorous

control of diet, usually possible only in a Clinical Research Center. Because this approach, case by case, is too costly to be practical, it is my recommendation that population-wide sodium restriction should be recommended. The statement of the American Academy of Pediatrics in 1974, "salt is but one example of a nutrient that can be enjoyed by many, but must be restricted in some" [4] assumes that the "some" can be identified in a practical fashion. The Academy concludes their statement by the thought that "dietary modification for persons at risk, rather than for the population at large, is consistent with sound medical and epidemiological practices". In 1988 we still do not have the ability to identify those individuals who are truly "pre-hypertensive". The cost of the determination of salt-sensitivity, probably only one of many factors which enter into the evolution of EH, is prohibitive. Because the diet of children and adults in the United States far exceeds the upper limit of the "safe" levels published in the Recommended Dietary Allowances, and much farther exceeds the physiologic need for sodium (by 20-60 times!) the most stringent recommendation for sodium restriction could not lead to problems in healthy adults or children. Further studies are needed to assess the long-term impact of significant sodium restriction beginning in infancy. Data available from studies of healthy children would suggest that there may be race-related differences in the evolution of, and thus the prevention of, EH [15]. The restriction of sodium in the Black population may be far more important in primary prevention than in the White population. Data available to date, however, would suggest that any level of sodium restriction which is palatable and does not lead to a decrease in caloric intake of growing infants and children will be safe for all and may be effective in the prevention of EH in some. We need to begin prevention programs now; the younger the target audience, the better.

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CAFFEINE AND HYPERTENSION

Italo Biaggioni, Edwin K. Jackson,
Rose Marie Robertson and David Robertson
Department of Pharmacology
Vanderbilt University
Nashville, TN

Caffeine is an important component in the usual American diet. It is present in coffee, tea, and chocolate, and these have been the most popular beverages in Western society for several hundred years. It is also present in many soft drinks and over-the-counter medicines (1). The annual world consumption of coffee exceeds four million tons. In some countries this amount translates into a per capita ingestion of 100 g of pure caffeine each year (2).

It is not surprising, therefore, that the potential health consequences of caffeine ingestion have been of great concern to the medical community and the general public as well. Paradoxically, the deleterious effects of caffeine are still uncertain, mainly due to the limited systematic study this issue has received. The list of adverse effects ascribed to caffeine is long, but a critical review of these suggests that caffeine does not seem to be associated with myocardial infarction, lower urinary tract infection, renal or pancreatic cancer, teratogenicity, or fibrocystic breast disease. A minor role of caffeine in the production of hypertension, cardiac arrhythmias and gastric or duodenal ulcers remains possible (3). We will present the existing data on the cardiovascular effects of caffeine ingestion, the proposed mechanism of action of caffeine, and discuss recent studies from our group which document its adverse effects in experimental renovascular hypertension.

Cardiovascular Effects of Caffeine

Earlier studies showed contradictory cardiovascular effects of caffeine. Caffeine has been reported to raise (4,5), lower (6) and not alter (7) the arterial blood pressure; increase (6,8), decrease (5,9) and not alter (4,7) heart rate; and raise (2,10) or not alter (11,12) plasma catecholamine levels. This apparent contradiction can now be explained by the failure to distinguish between habitual consumers and nonconsumers of coffee, and the failure to standardize sodium consumption during these studies.

Most studies have given caffeine in the form of capsules, or with a hot caffeine-free beverage as a vehicle. It has been shown that the cardiovascular effects of drinking coffee are mainly the result of its caffeine content, since decaffeinated coffee has no significant hemodynamic effects (13), and the cardiovascular effects of coffee and caffeine are indistinguishable (14).

Because of caffeine's widespread use and the limited systematic study it had received, the cardiovascular effects of caffeine have been a long-term interest of our group. In healthy volunteers, we showed that caffeine acutely raised blood pressure (15). The equivalent of 2 cups of strong coffee (250 mg) was given orally to nine healthy caffeine-naive subjects, in a double-blind, placebo-controlled study. Caffeine increased both systolic and diastolic blood pressures. The maximal change was seen one hour after caffeine, when a mean increase of 14/10 mmHg was observed ($p<0.05$ compared to placebo) (Figure 1). Increases in plasma catecholamines as well as plasma renin activity were also seen.

The effects of caffeine on cardiac output are also controversial,and studies are few. Gould showed an increase in cardiac output and stroke volume in five normal subjects undergoing cardiac catheterization (8). However, a later double-blind, placebo controlled study showed an increase in calculated systemic vascular resistance but no increase in cardiac output or contractility. The latter, how-

ever, was determined only indirectly using systolic time intervals (16). Thus, it is unclear whether the pressor effect of caffeine is due to an increased cardiac output and an increase in systemic vascular resistance, or to an increase in vascular tone alone.

To determine if tolerance developed to the hemodynamic effects of caffeine, we studied 18 healthy subjects brought to sodium balance (150 mEq/day), and examined the effects of caffeine both acutely and during prolonged administration (14 days). Caffeine, 250 mg orally with each meal, acutely increased both systolic and diastolic blood pressures. However, near complete tolerance, in terms of both humoral and hemodynamic variables, developed over the first 1-4 days of caffeine. The blood pressure returned to baseline levels by day three (Figure 2). No long-term effects of caffeine on blood pressure, heart rate, plasma renin activity, plasma catecholamines, or urinary catecholamines could be demonstrated. Discontinuation of caffeine ingestion after 7 days of administration did not result in a detectable withdrawal phenomenon relating to any of the variables assessed (17).

Mechanisms of Action of Caffeine

The underlying mechanisms for caffeine's actions are not completely understood. Caffeine has phosphodiesterase inhibitory activity, resulting in increased intracellular levels of cAMP. It can also mobilize intracellular calcium. However, the concentrations needed to show these effects are higher than those usually achieved in vivo (18). There is increasing evidence that caffeine and other methylxanthines may exert their actions through a competitive antagonism of adenosine receptors (18-20). Adenosine is a potent vasodilator both in vitro (21) and in vivo (22), acting on specific vascular receptors (23,24). Adenosine also inhibits norepinephrine release through presynaptic receptors (25-27), and inhibits renin release (28-30). More importantly, perhaps, adenosine can act on the nucleus tractus solitarii and the area postrema, centers in the brainstem involved in cardiovascular control, to produce hypotension (31). These actions are mediated through cell surface receptors and therefore are dependent on extracellular adenosine concentration. Two types of receptors have been identified (32). Ra receptor stimulation is associated with activation of adenylate cyclase and cAMP accumulation. Ri receptor stimulation is associated with inhibition of adenylate cyclase and will blunt receptor-mediated cAMP accumulation. The actions of adenosine on Ri inhibitory receptors in general can be demonstrated more clearly after activation of the system (for example, adenosine will inhibit renin release due to -receptor activation, prostaglandins or ischemia; adenosine will inhibit norepinephrine release due to electrical stimulation). Both receptor types are blocked with the same efficacy by methylxanthines like caffeine. Furthermore, chronic caffeine consumption in rats has been shown to produce down-regulation of adenosine receptors in the brain (33).

Caffeine in Borderline and Essential Hypertension

Although it was reassuring that sustained caffeine ingestion did not adversely influence blood pressure in normal subjects, it remained possible that hypertensive patients might be more sensitive to the pressor effect of caffeine than normal subjects. For this reason, we tested 18 patients with borderline hypertension in a double-blind placebo-controlled study similar to that described above. Systolic blood pressure increased 9.2 Ò 3.4 mmHg within 15 minutes after the first dose of 250 mg caffeine. On the first day of caffeine, systolic pressure was increased a mean of 7.3 Ò 4.0 mmHg, but the increase was no longer significant after the initial day of caffeine administration. Plasma catecholamines and plasma renin activity increased, but did not reach significance on either a short- or long-term basis. After seven days of caffeine, systolic blood pressure was slightly above baseline, but was not significantly different (Figure 3). After discontinuation of caffeine, blood pressure returned to baseline. No overshoot phenomena were observed (34).

Caffeine in Experimental Renovascular Hypertension

Thus, in normal subjects as well as borderline hypertensives, caffeine exerts a pressor effect. However, the increase in blood pressure is not

sustained, due to the development of tolerance. The mechanism of this pressor response is not clearly defined. It may well be multifactorial, with at least some of the effect related to adenosine receptor blockade. Caffeine clearly activates the sympathoadrenal system, and although this may be a contributing factor, the pressor responses after caffeine ingestion do not bear a simple relation to the increment in either norepinephrine or epinephrine levels (Figure 4). A pressor response is also seen in patients with autonomic failure (35). Caffeine also increases plasma renin activity. The extent of this activation may be dependent on dietary sodium intake and prior plasma renin activity levels. It seemed possible then, that the pressor response to caffeine could be different in a situation where plasma renin activity is high and the potential importance of its modulation by caffeine is greatest. A classical model for this is renovascular hypertension. We theorized that during renal ischemia the levels of endogenous adenosine would be increased. It has been proven that adenosine inhibits the release of renin due to different stimuli, among them renal ischemia (29). Therefore, caffeine, being an adenosine receptor antagonist, might exacerbate renovascular hypertension by preventing endogenous adenosine from attenuating the renin response to renal artery stenosis.

This hypothesis was tested in a rat model of renovascular hypertension. The effects of long-term administration of caffeine on blood pressure were determined in two-kidney, one clip rats and compared to those observed in sham-operated rats and spontaneously hypertensive rats (36). Animals were randomly assigned to receive either 0.1 percent caffeine in their drinking water or normal drinking water. Systolic blood pressure was monitored for 6 weeks using a photoelectric tail cuff method.

As in normal human subjects, chronic caffeine administration did not alter systolic blood pressure, plasma renin activity or creatinine in sham-operated rats (Figure 5). Caffeine also had no significant effect on plasma renin activity after 6 weeks. Rats fed a normal diet had a plasma renin activity of 1.8 Ò 0.4 ng AI/ml/hr compared to 1.9 Ò 0.4 in caffeine-fed sham-operated rats. Also, in agreement with our previous findings in borderline hypertensives, chronic caffeine had no pressor effect in spontaneously hypertensive rats (SHR), the animal model that most closely resembles human essential hypertension.

In sharp contrast, caffeine markedly exacerbated the severity of hypertension in 2 kidney-1 clip (2K-1C) rats, the animal model that most closely resembles human renovascular hypertension. Two-kidney one-clip rats were fed caffeine immediately after surgery. After 6 weeks, systolic blood pressure in this group of rats was 219 Ò 4 mmHg as compared to 169 Ò 5 mmHg in 2K-1C, non-caffeine control group (Figure 5). This exacerbation of blood pressure was associated with an enhanced plasma renin activity. In the no-caffeine group, plasma renin activity after 6 weeks was 4.4 Ò 0.5 ng AI/ml/hr, a 2.4-fold increase compared to sham-operated rats, and an expected increase due to renal artery clipping and renal hypoperfusion. However, in caffeine-fed renovascular hypertensive rats, plasma renin activity at 6 weeks was 31.8 Ò 7.8, a 7-fold increase when compared to renovascular rats on a normal diet. That caffeine-induced exacerbation of hypotension was due to enhancement of the renin-angiotensin system is supported by that fact that chronic treatment with enalapril, an enzyme converting inhibitor that prevents angiotensin II accumulation secondary to the increase in renin activity, prevented the development of hypertension in 2K-1C control rats and 2K-1C caffeine-fed rats. Furthermore, withdrawal of enalapril precipitated a rapid rise in systolic blood pressure in caffeine-fed but not in control rats (Figure 6).

None of the rats in the no-caffeine diet died. In contrast, 3 of the 8 rats in the caffeine group died. There was histological evidence of malignant hypertension in these animals. No tolerance to the effects of caffeine was seen.

The mechanism of action of caffeine seems to involve blockade of adenosine receptors. In favor of this hypothesis are the facts that 1) adenosine is a potent inhibitor of renin release (29); 2) plasma levels of adenosine are greatly increased in 2K-1C but normal in non-renin dependent hypertension models (37); 3) the amount of caffeine in the diet produced plasma levels of 10 %g/ml in these rats, comparable to those found in heavy coffee drinkers. The same caffeine intake was shown to effectively block the cardiovascular effects of exoge-

nously administered adenosine (26); and 4) the effects of caffeine in renin release are shared by other methylxanthines which are highly specific adenosine receptor agonists (38).

Implications and Conclusions

The finding that caffeine exacerbates experimental renovascular hypertension raises critical questions. To what extent, if any, does caffeine exacerbate human renovascular hypertension? Is the pressor response to caffeine also enhanced in other high-renin states? Although these results should not be extrapolated hastily to people, they do underscore the need for careful clinical studies to address these questions.

Renovascular hypertension is the most common cause of secondary hypertension. Estimates of prevalence vary over a wide range, from 100,000 to 1,200,000 in the United States. Improved detection techniques might reveal this number to be considerably higher. Most importantly, the prevalence of renovascular hypertension is much higher in the group of patients with severe hypertension. The prevalence of renovascular hypertension among all hypertensives is approximately 5 percent. However, its prevalence among patients with malignant and accelerated hypertension is at least 23 percent (39). Since the use of caffeine in the diet is so widespread, it is critically important to determine its potentially deleterious effects in patients with renovascular hypertension. Inasmuch as these patients frequently present with severe hypertension, they will be particularly at risk for further exacerbation of their hypertension.

In summary, although the list of potential deleterious effects of caffeine is long, most of them remain doubtful. Regarding its effects on blood pressure, caffeine produces an acute increase in blood pressure in caffeine-naive normotensive subjects, but blood pressure returns to normal in one or two days with continuous caffeine ingestion. This is probably explained by the development of tolerance to the acute effects of caffeine. The same phenomenon is observed in borderline hypertensives. It seems, therefore, that caffeine consumption probably does not adversely affect blood pressure in these populations. However, recent data in experimental animals have shown that caffeine greatly exacerbates hypertension in a renovascular model of hypertension. It is not yet known whether these results can be extrapolated to human renovascular hypertension. It seems prudent, however, to consider asking patients with this form of hypertension to abstain from caffeine-containing beverages until its effect on their blood pressure is determined.

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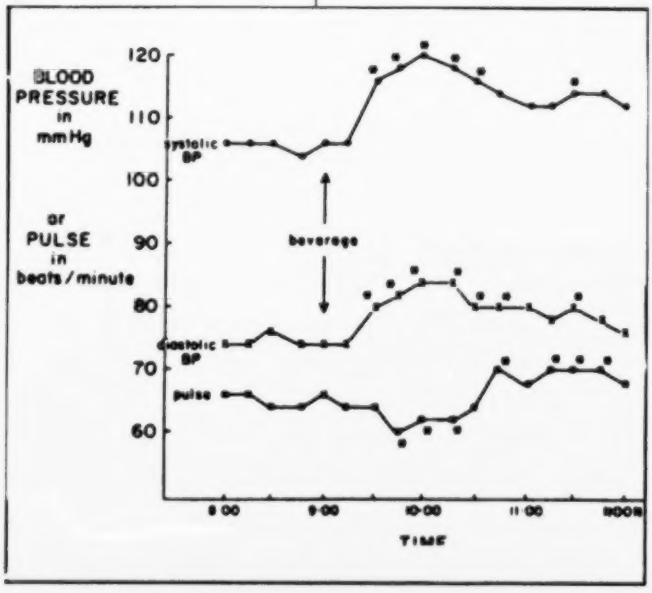

Figure 1. Mean blood pressure and pulse after caffeine. *p<0.05 compared with measurements after placebo. (Adapted from Robertson D et al (13) with permission from the editors.)

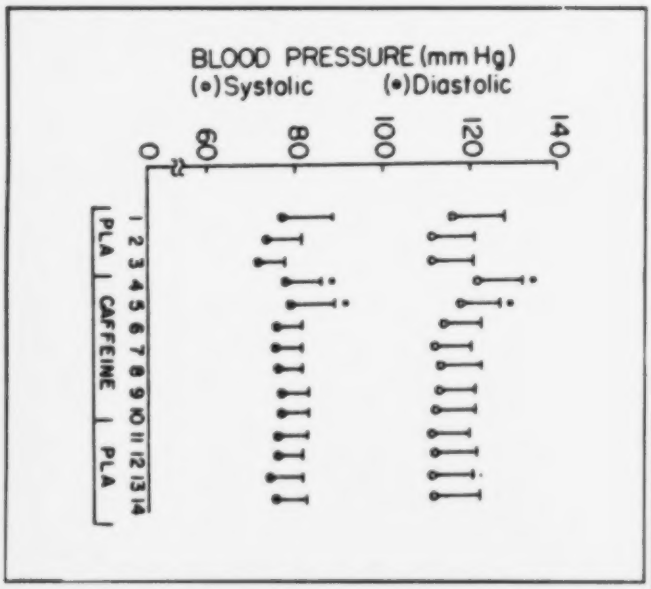

Figure 2. Blood pressure response to caffeine. Numbers on the horizontal axis indicate the day of the study. On days 1-3, subjects were given placebo beverage with each meal. On days 4-10, they received 250 mg caffeine with each meal. On days 11-14, they again received placebo. Each point represents the mean of six upright and six supine sphygmomanometric systolic (o) and diastolic (o) blood pressure determinations. *p<0.05. (Adapted from Robertson D et al (17) with permission from the editors.)

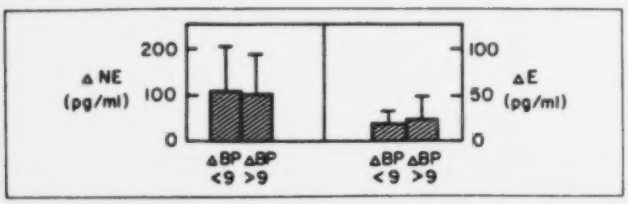

Figure 4. Relation of blood pressure increments to norepinephrine stimulation in subjects with borderline hypertension. The hatched bars show incremental response in plasma norepinephrine levels in short-term caffeine administration in persons whose blood pressures rose less than 9 mmHg and in persons whose blood pressures rose more than 9 mmHg. In the right half of the illustration, the respective data for epinephrine increment are shown. It can be seen that the increase in blood pressure after caffeine ingestion does not bear a simple relation to the increment in either norepinephrine or epinephrine levels. (From Robertson D et al (34) with permission from the editors.)

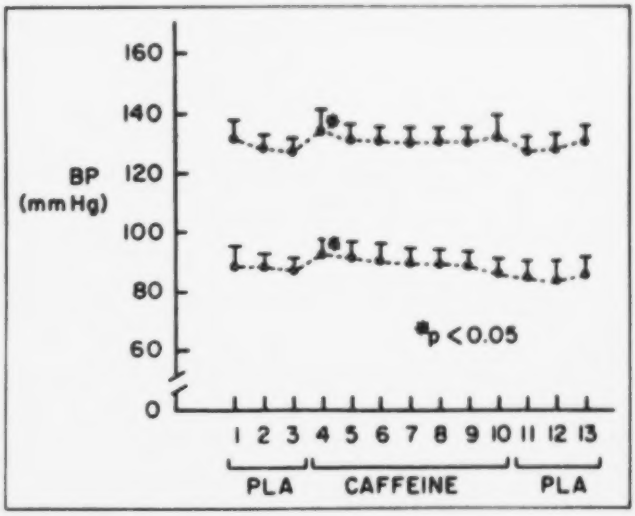

Figure 3. Long-term effect of caffeine on blood pressure in subjects with borderline hypertension. The x-axis shows the day of the study. During the first three days and the last three days, placebo was given. During Days 4 to 10, caffeine (250 mg) was given three times daily. Blood pressure was determined in the supine and upright postures before and after breakfast and lunch. Thus, each point represents eight blood pressure determinations for each of the nine subjects on each day. (Adapted from Robertson D et al. (34) with permission from the editors.)

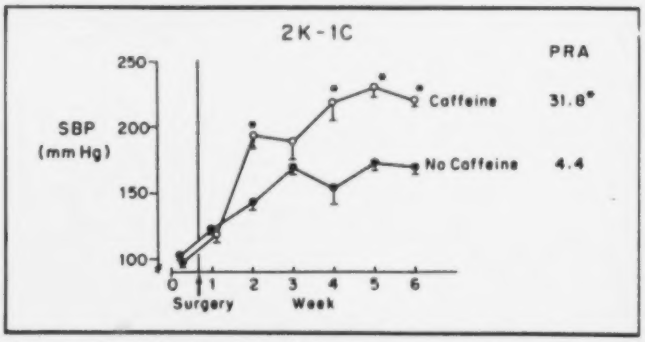

Figure 5. Effects of caffeine vs normal drinking water in 2 kidney-1 clip rats (2K-1C) (renovascular hypertension). PRA=Plasma renin activity (ng AI/ml/hr). (From Ohnishi A et al (36) with permission from the editors.)

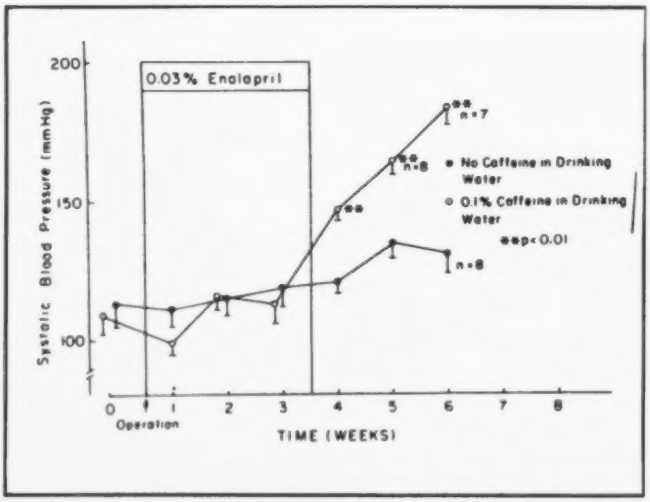

Figure 6. Effect of enalapril on blood pressure in renovascular hypertensive rats (2K-1C) treated with caffeine (open circles) or normal drinking water (closed circles). (From Ohnishi A et al (36) with permission from the editors.)

PREVENTION OF HYPERTENSION THROUGH DIET: RESEARCH PRIORITIES

Paula C. Zemel*,
Michael B. Zemel and
James R. Sowers
Department of Medicine and Nutrition
Wayne State University Medical School
Detroit, Michigan

ack-white death gap due to hypertension- associated morbidity and mortality is a goal of both researchers and clinicians involved in basic and applied research, community program development and evaluation and management of hypertensive patients. Currently, cardiovascular diseases account for approximately 50% of all deaths and half of these deaths are attributable to environmental risk factors (Table 1) (1). Thirty percent of these deaths have been ascribed to dietary excess (i.e. calories, salt, fat) and an additional 5-10% to alcohol abuse (1). Thus, nutrition is an important component in cardiovascular disease research including hypertension.

Current dietary recommendations for the control and prevention of hypertension include weight control, alcohol restriction and salt restriction for salt-sensitive individuals (2). At present, knowledge about other dietary constituents, such as fat, protein, sucrose and caffeine is too fragmentary to make general recommendations about their use in prevention and treatment of hypertension. In addition, dietary practices and factors which influence these habits have not been adequately evaluated in black communities. Thus, research priorities on the role of nutrition in the prevention and treatment of hypertension among blacks include: 1) the role of cations and salt sensitivity, 2) preventing and controlling obesity, and 3) promoting healthy dietary practices.

Role of cations and salt sensitivity

Dietary cations, including sodium, potassium, magnesium and calcium appear to exert significant effects on blood pressure regulation (3-6). However, only limited data are available regarding the effects of these cations in salt sensitive states, as is characteristic of hypertension in blacks and the elderly (7). Specific data regarding these cations in blacks is especially lacking, although recent research in this area has focused on the effects of salt and calcium.

High salt diets can increase vascular resistance through several mechanisms. Although dietary salt has been reported to be similar in blacks whites (3,7) blacks appear to exhibit a higher sensitivity to dietary salt (3,8,9).

High dietary salt intake may increase vascular smooth muscle tone via effects on vasoactive hormones and cellular cation transport systems and may increase responses to vasoconstrictor stimuli by increasing cellular sodium, calcium and water content and the wall to lumen ration of blood vessels (10-12).

An enhanced degree of salt-sensitivity in the black population may result, in part, from an enhanced renal retention of sodium even under salt loading conditions (8,11). This phenomenon is also seen in the elderly (2). Intracellular sodium levels are increased in leukocytes and erythrocytes of people with essential hypertension (13,14). Abnormalities in Na-K ATPase, Ca-ATPase and calcitropic hormones may also be partially related to the high incidence of salt sensitivity in blacks (12,15).

Suboptimal calcium intakes may play a role in the genesis and maintenance of hypertension,

particularly in the low renin, salt-sensitive state in humans and in animal models of hypertension (12,15,16,17). Decreased levels of both serum ionized (18,19) and total calcium (20) have been reported in patients with essential hypertension compared to normotensives. Similar changes have been shown in animal models (16,17), and in both human and animal studies, increasing dietary calcium reduces blood pressure. Abnormalities in calcium metabolism leading to blood pressure elevations have been reported in blacks in response to salt loading (12,15,21,22). Furthermore, increasing dietary calcium into normal ranges in black salt-sensitive individuals to attenuate these salt-induced changes in calcium metabolism and consequently lowers the blood pressure response to increased salt (3,12,21,22).

Our investigative group has reported that increasing the calcium intake of either normotensive or hypertensive blacks by 600 mg/day in the form of yogurt reversed the salt-induced elevations in blood pressure found on low calcium diets (Table 2) (3,22). We have also found that increasing dietary salt at low calcium intakes in low-renin salt-sensitive black hypertensive results in increased serum PTH and urinary cyclic AMP excretion as well as increased blood pressure (Tables 3, 4). Thus, dietary calcium appears to exert an antihypertensive effect in salt-sensitive blacks by minimizing the effects of sodium chloride on calcium metabolism and blood pressure regulation (3,12,22).

In addition, we have recently shown dietary calcium supplementation to be effective in regressing left ventricular hypertrophy in black hypertensives (Table 5) (23). The effect of calcium was comparable in magnitude to that previously reported for several antihypertensive agents (24-26) as well as extended weight loss (27). Although the effects on left ventricular function and long term morbidity and mortality are unclear, this represents an area where nutrition may be associated with reduction of significant secondary complications of hypertension.

Research priorities in this area clearly must extend these findings to determine optimal levels of calcium and sodium intake for maintenance of normal blood pressure in blacks. Interactions of these minerals with potassium and magnesium have not been investigated. In addition, the interaction of these minerals with other dietary factors is currently poorly understood and must be evaluated. Further, the role of dietary cations in underlying factors associated with cardiovascular disease morbidity and mortality needs evaluation.

Weight Control and Hypertension

Obesity is a major cardiovascular risk factor for blacks in the U.S. and is most prevalent among black women (Figure 1) (28). In black women, hypertension, mortality due to heart disease, stroke and diabetes occur at rates 1.5-2.5 times rates for white women (29). However, the excess health risk for black women due to cardiovascular disease mortality, hypertension, diabetes, elevated serum cholesterol and other obesity-related diseases such as osteoarthritis is not proportionate to excess obesity compared to white women (30). Thus, the prevention and control of obesity in black women is a major public health concern to be addressed.

Genetic, socioeconomic and environmental factors are also important in evaluating the prevalence of obesity. Genetic factors are well-accepted, but are difficult to differentiate from environmental influences in human studies since there is a disproportionate prevalence of obesity in blacks of lower socioeconomic status (31,32). Since more women fall into lower socioeconomic strata, it is difficult and may be impossible to separate culturally-based factors from social class factors which influence obesity. For example, fewer blacks were classified as health conscious eaters (using yogurt, fruit and cottage cheese) than whites in a study of food preferences of middle class women (33).

The role of environmental factors in obesity in black women is also unclear. In addition to exercise, perinatal factors, permissive attitudes toward obesity and food preferences have been suggested as factors which may be associated with increased obesity among blacks (30).

The role of obesity as a risk factor in the development of hypertension in middle class blacks was clearly illustrated in the Meharry study (34). This study eliminated the influences of socioeco-

nomic status in a primarily male cohort and underscored the contributory role of obesity to black hypertension. Results of this study have been supported by data from other investigators (35).

Most research on obesity in black population, has been descriptive and there have been few reports concerning prevention and treatment. A study of elderly blacks in Washington D.C. showed that a weight control and exercise program was successful in promoting these health-conscious behaviors (36). Research on cultural, socioeconomic and genetic factors associated with obesity in blacks, especially black women is clearly needed. Research paradigms using twins, as suggested by Grimm (37), would be an especially efficient method for exploring some of these issues. Additionally, the need for data on these factors in the general black population, including both obese and non-obese indivduals, should be considered in the design of national health surveys and other studies.

Promoting Healthy Dietary Practices in Black Communities

Scientific participants at this conference have reviewed our current knowledge of several nutrients and their relation to hypertension. Some blacks may consume inadequate quantities of these nutrients, such as calcium, potassium and magnesium or too much of other nutrients, such as saturated fat due to cultural or other factors affecting food selection. Some blacks may also handle nutrients such as salt differently, thus contributing to salt sensitivity and the associated increased prevalence of hypertension.

Differences in dietary patterns between blacks and whites in the United States have been observed. One study indicated that black children consumed more calories, fat and cholesterol than white children (38). In another study, black adult women consumed more poultry, fish and shellfish, frankfurters, luncheon meats and sausages, eggs, dark green vegetables and grain products, than white adult women (39). These women also had lower intakes of dairy products, fruit, fats and oils and sugar and sweets than white adult women. These differences contributed to lower intakes of calcium, magnesium, zinc, folacin, vitamin B_2, and vitamin E among black women although both black and white women feel short of the RDA for these nutrients (40). Black adult men also had lower intakes of vitamin B_6, calcium, magnesium, vitamin E, folacin, zinc, vitamin A and riboflavin than white men (41). Some of these differences may also be due to the influence of traditional food patterns in the southeast United States (42).

Life-styles, associated with lower risk of hypertension have been shown to be associated with lower blood pressure in blacks. Black Seventh-Day Adventist vegetarians had lower blood pressure and took fewer antihypertensive medications than nonvegetarians (43). However, health promotion programs have generally not been targeted to ethnic populations. For example, Storer et al (44) determined that recipes recommended by the American Heart Association included many foods that were not available in central Mississippi, and individuals in this area could not easily apply these health promotion materials to change their diets. Thus, in order to promote changes in dietary patterns, health promotion materials must be tailored to consider cultural, geographic and other factors which may be related to the propensity for behavioral change.

The development and evaluation of programs which promote dietary practices associated with lower health risks are needed in the black community. We have shown that black males were able to increase their calcium intake by adding 2 cups of yogurt to their diet daily (3). Some of these men continue to include yogurt in their usual diet since completing our studies (45). Thus, health promotion programs should be based on modifying existing cultural patterns to alter mineral, fat and calorie intakes in adults and encourage the development of health conscious low risk dietary patterns among children.

Research priorities in this area include the identification of methods of dietary change which promote these modifications. Programs should be based on current theories of behavioral change. For example, the use of social marketing theory has been associated with successful health promotion programs (46). Health promotion programs should also use accepted evaluation methods and should consider validity and reliability in dietary, biochemical and psychosocial assessments.

Future Research Directions

The impact of nutrition on hypertension and cardiovascular disease in blacks is complex. Our interpretation of current reseach must consider genetic differences as well as cultural, socioeconomic and geographic factors which may influence food choices. The synthesis of current research on nutrition and hypertension in blacks from various international and U.S. studies is difficult and it is impossible to make generalizations.

Future research must recognize the heterogeneity of the hypertensive population as well as that of the black population. Our research agenda should consider basic science, clinical, and epidemiological approaches to understanding genetic, cultural and socioeconomic factors which clearly are related to diet and hypertension (Figure 2). By unraveling the interrelationships among these variables, we can use diet to help prevent and treat hypertension, reduce cardiovascular disease morbidity and mortality and close the black-white death gap.

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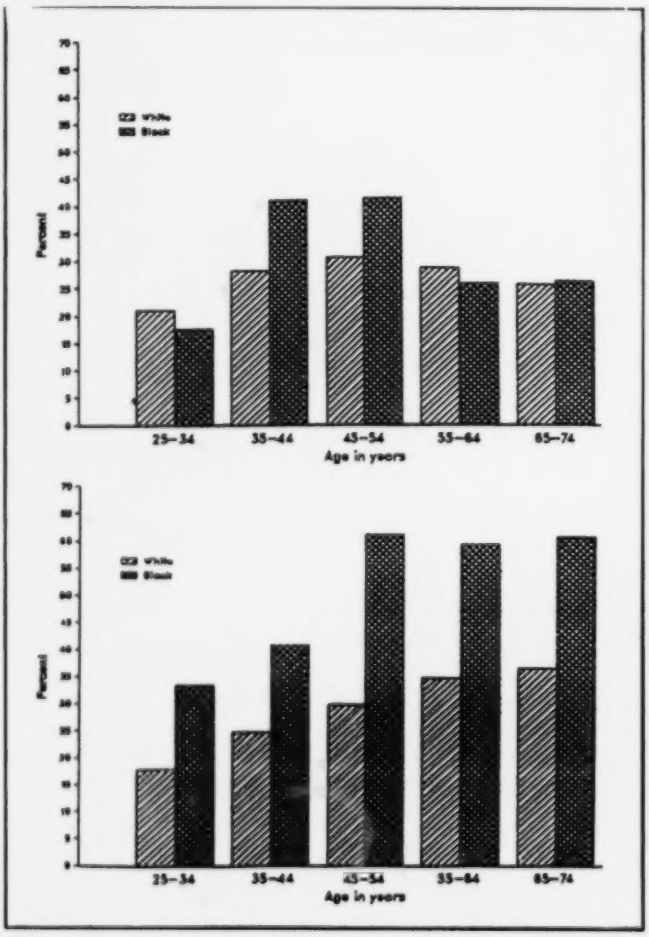

Figure 1. Percent of males (top panel) and females (bottom panel) overweight by race and age: 1976-80. Source: Joint Nutrition Monitoring and Evaluation Committee. Nutrition Monitoring in the U.S. (DHHS Publication No. (PHS) 86-1255). Hyattsville, MD, DHHS and USDA, 1986, p59.

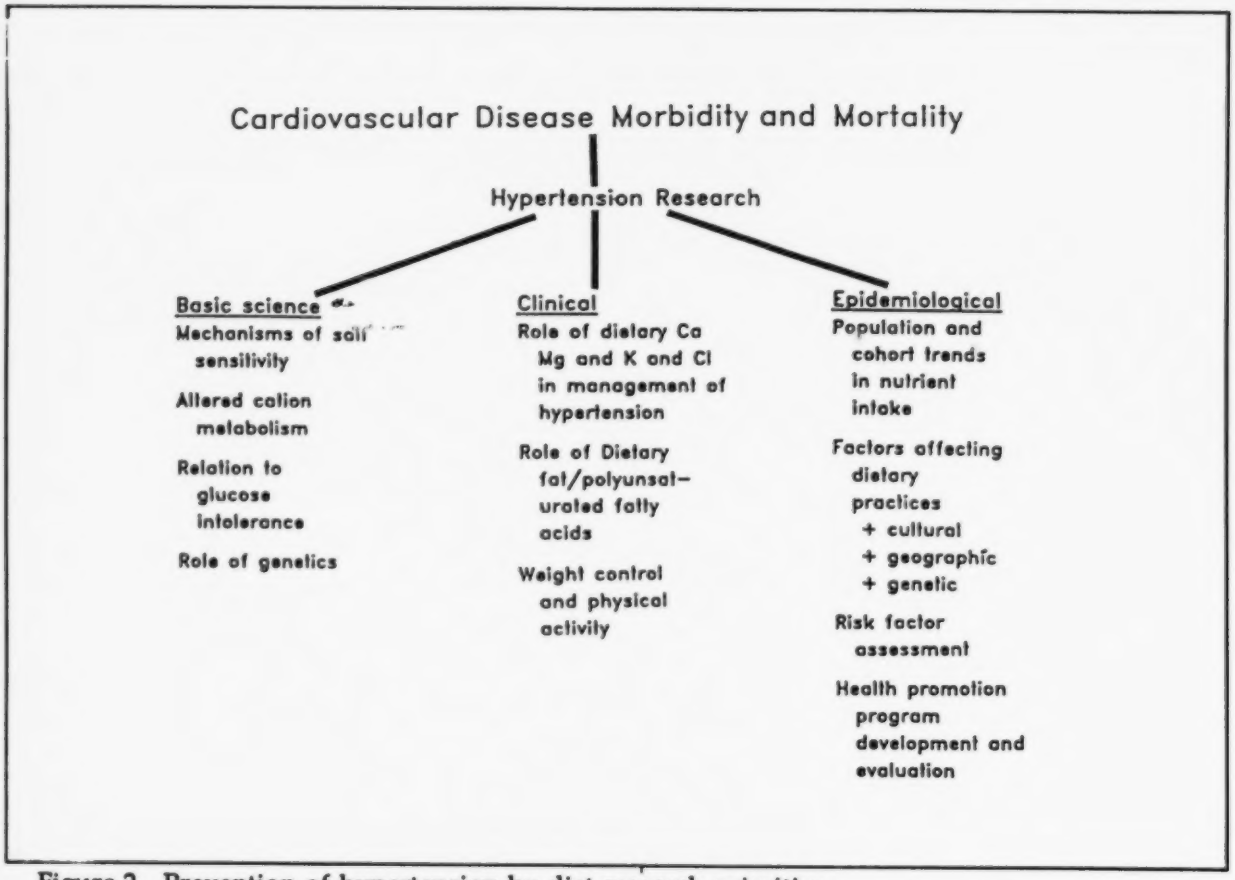

Figure 2. Prevention of hypertension by diet-research priorities.

Table 1
Selected risk factors and estimates of the percentage of their contributions to all annual deaths due to cardiovascular disease.

Risk Factor	Deaths Attributable to Risk Factor %
Cigarette smoking	30
Air pollution	1-5
Diet excess	30
Diet deficit	+
Hazardous worksite	1-5
Alcohol abuse	51
Non-medical drugs	1-5
Hypertension	50
Percent deaths attributable to risk factors	50
Percent of total deaths	51

+ = contributory to an unknown extent
Source: Office of Disease Prevention and Health Promotion, Integration of Risk Factor Interventions. Washington D.C.:
U.S. Public Health Service, 1986, pg 59.

Table 2
Urinary calcium and sodium excretion in hypertensive black adults an affected by dietary calcium and sodium.

	Diet			
Mineral	356 mg Ca 1000 mg Na	356 mg Ca 4000 mg Na	956 mg Ca 1000 mg Na	956 mg Ca 4000 mg Na
Calcium (mg/day)	154.9^{a} $\pm$ 7.7	168.0^{b} $\pm$ 6.4	153.2^{a} $\pm$ 7.8	178.9^{b} $\pm$ 7.7
Sodium (mg/day)	653^{a} $\pm$ 34	4503^{b} $\pm$ 304	1027^{c} $\pm$ 72	5986^{d} $\pm$ 397

Non-matching superscripts in each row denote significant ($p<0.05$) differences.

Adapted from Zemel et al. Am J Hypertension 1:70-72, 1988 (Ref. No. 21) and from Zemel et al., J Hypertension 1986 (Ref. No. 3).

Table 3
Effects of dietary calcium and sodium on supine systolic and diastolic blood pressure in salt-sensitive black subjects.

	Treatment			
Measurement	Low Ca Low Na	Low Ca High Na	High Ca Low Na	High Ca High Na
Systolic pressure (mm Hg)	128 ± 4[a]	141 ± 5[b]	129 ± 4[a]	132 ± 5[a]
Diastolic pressure	80 ± 4[a]	84 ± 4[b]	80 ± 3[a]	80 ± 4

Non-matching superscripts in each row denote significant ($p<0.05$) differences.

Adapted from Zemel et al, J Hypertension 1986 (Ref. No. 3).

Table 4
Serum mid-molecule parathyroid hormone and erythrocyte intracellular calcium in hypertensive blacks as affected by dietary calcium and sodium.

	Diet			
Measurement	Low Ca Low Na	Low Ca High Na	High Ca Low Na	High Ca High Na
PTH (ng/ml)	0.59[a] ± 0.08	0.65[b] ± 0.10	0.58[a] ± 0.11	0.55[a] ± 0.13
Intracellular calcium (Ûg/ml cells)	2.16[a] ± 0.27	4.43[b] ± 1.47	2.36[a] ± 0.27	2.20[a] ± 0.30

Non-matching superscripts in each row denote significant ($p<0.05$) differences.
Adapted from Zemel et al Am J Hypertension 1988 (Ref. No. 22).

Table 5

Table 5
Effect of calcium supplementation on left ventricular mass, left ventricular diastolic dimension, mean arterial internal pressure, forearm blood flow and vascular resistance in black type II diabetics with hypertension.

Parameter	Pre-calcium	Post-calcium
LV mass (g)	346 ± 31	290 ± 30*
LV diastolic dimension (mm)	53.5 ± 2.7	47.8 ± 2.6*
MAP (mm Hg)	121 ± 4	114 ± 3*
FVR (mmHg/[ml/min/100ml])	31.8 ± 2.7	25.3 ± 2.3*
FBF (ml/min/100 ml)	3.8 ± 0.5	4.5 ± 0.7*

* ($p<0.05$) Significantly different from pre-calcium treatment.

Fifth Scientific Session - Discussion

Dr. Ernst:
Your findings on reactivity, I might add are perfectly consistent with the data we presented. Would you care to speculate on the possible mechanisms with specific regard to reactivity and the calcium balance.

Dr. Alpert:
I really wish I know the answer to that, Fred. Unfortunately, we have not done any studies that would try to dissect out the differences. What we are doing now in our second stage of our grant is taking hyperreactors, supplementing them with calcium to see if, in fact, we can reduce reactivity and if we can, then we will go back to look at their erythrocyte sodium pump activity and other biochemical markers. But I am sure Herb Langford would probably be able to answer the question better than I - I really don't have any mechanistic approach right now other than I am sure, as Paula's work has shown, you would have to get to the cellular mechanism, to the smooth muscle cell, to the autonomic nervous system, it is a very complex answer, I am sure.

Dr. Ernst:
One other follow-up question - were there any differences between the high and low calcium subjects in resting blood pressures, in which case there would be different baselines prior to the reactivity testing?

Dr. Alpert:
No, there were no significant differences; there was a very small difference, but it wasn't even close to significance.

Dr. Ernst:
Exactly what we found, as well.

Anonymous:
(Question inaudible)

Dr. Alpert:
The reasons for our studies primarily in healthy children are to define what we can see in screening a healthy, large population of individuals and fit together a risk factor assessment. As Fred's work has shown as well, if you take a group of normotensive healthy children, their blood pressures at rest - and I have some exercise data that I could show as well - but the resting blood pressure is not a very good predictor of blood pressure many years later. The reason to do reactivity assessments, whether they be to a psychological stressor, a physical stressor, to what we call stress of everyday life, with 24-hour ambulatory monitoring, is to try to pick out some markers or screening tools that can be used. In other words, if you tweak the system a little bit from rest, there are going to be individuals who are going to be high reactors to one or several of the stressors, and those children, are possibly the ones at highest risk for hypertension later in life.

Clearly, your points are very well taken about clinical pediatrics and calcium nutritional status. The purposes of our study are really to define in the general population what can be done and what can be designed for the health maintenance person, let's say the school nurse, if there are

school nurses anymore, or the person who could work in the pediatrician's or public health department offices and deliver a very simple test. It takes about eight or twelve minutes. You measure a couple of blood pressures. If that is a sensitive indicator of hypertension later in life, then that individual can be entered in a much more rigorous protocol. As we were discussing during the break, those individuals who are at highest risk because they are black and have hypertensive parents can have extra time devoted to them from infancy on through childhood, adolescence and adulthood.

Our calcium studies are really very primitive and only circumstantial. But what we are trying to do is design large scale screening techniques for prediction of hypertension in later adult life.

Dr. Carter:

Bruce and Paula, is this reactivity related to intracellular calcium?

Dr. Zemel:

I had better pass it - we haven't done any reactivity work at all.

Dr. Alpert:

We haven't done any intracellular calcium work. This is a Mexican standoff, if you will excuse the expression. I really don't know.

Dr. Zemel:

It is a very good question, though.

Dr. Grossman:

I have a comment for the caffeine expert and a challenge for Dr. Zemel. The comment on the caffeine is that the real crucial issue is whether chronic caffeine ingestion is related to the disease essential hypertension. The acute elevation of blood pressure that is seen in caffeine-naive subjects is not very different from the fact that my blood pressure is up now because I am speaking to you - that is, it has been measured and shown that giving a speech raises the blood pressure. In fact, you don't even have to vocalize because I have found a paper which shows that deaf mutes who sign have an elevation of their blood pressure while they are signing.

Needless to say, there are countless activities that one engages in every day, like running up a flight of steps, and so forth and so on, which temporarily raise one's blood pressure. It is a condition of life.

The basic issue is whether there is there a relationship between chronic coffee consumption or caffeine consumption from any source, be it tea, Coca-Cola, hot chocolate, and so forth, and the disease known as essential hypertension? There have been many epidemiologic studies which have attempted to answer this question. A few of them have come out positive; many more have come out negative. The one that I like to watch the most is the Framingham study, and Drs. Casteli and Cannell repeatedly state that there is no relationship between chronic coffee consumption and the disease essential hypertension. So I just want to make that point in that context.

Dr. Zemel, the challenge for you is this: I have been a physician for a very, very long time, and I have had a variety of practice experiences. For the past twelve years I have had the good fortune of being the employee health physician for a technical center in General Foods in Tarrytown, ministering to anywhere from 350 to 600 middle class black or white employees, usually with good education.

It has been my lifelong experience as a physician that, while I wholeheartedly agree with you that the natural way is the best, that if we could do what Oliver Wendell Holmes said about medicine - you remember he said, "If we took all the medications that are taken by mankind and threw them in the ocean, it would be so much the better for mankind and so much the worse for the fishes."

Anonymous:

New York City is already doing that.

Dr. Grossman:

And I believe in that, and I always appeal to patients to try the natural way. But I have found that the appeal of a pill always wins out. Almost without exception, if you tell people that they can't have cold cuts, potato chips, Big Macs, and so forth, they get very unhappy, and almost all of them, even though you tell them that if they take diuril, they may run the danger

of having elevated cholesterol, elevated blood sugar, elevated uric acid, they would rather do that than follow a diet. So the challenge is - one last thing I have the advantage of having a registered dietitian who is paid by General Foods to counsel employees, so I can call her and set up an appointment and she will sit with them for an hour - that is something I couldn't do when I was out in private practice. But with all of these advantages, I personally have not found a way to get people on a permanent basis to follow dietary rather than pharmacological practices in the treatment of hypertension. I wonder what your thoughts are?

Dr. Zemel:

It is a tall order. I think that clearly there needs to be some sort of concerted effort. With the number of nutritionists in this country - I think that if you look at public health standards, state public health departments are supposed to have one nutritionist for every 45,000 people, or something; the impact such a person can have is limited, and it is sort of overwhelmed by other noise, by other voices from food companies, etc., etc. I think what I would say, and I have to turn it back to you, is that we need to work in concert to identify - and I think we are seeing this happen to a certain extent now - the development of products that are appropriate and that are marketed appropriately. A Campbell's Soup person was telling me that the lower salt soups are selling very well. And I am glad to hear that. The no salt soups - and I tried buying them, they are expensive - I wouldn't eat them. The one-third reduced salt soups are delicious. I would like to see more herbs and less salt, but we are moving a step forward. I think we need to see the development of appropriate products and their advertising, and appropriate peer models within the community to promote their consumption.

Dr. Grossman:

Paula, allow me just one more question. If you go out and ask consumers what are their chief concerns about food - and this has been done by the government and by food companies - the number one concerns are sodium and cholesterol. Or, you go out to the supermarket, and you say, "What do you look for?" I wish someone would tell me why Ben and Jerry's ice cream and Hagen Daas ice cream are the biggest sellers. They have 16% butterfat. The standard identity for ice cream is 10% butterfat. There is sort of a schizophrenic attitude among consumers. I think most food companies say they feel if I've been good all day, I can sin at night, so if I'm going to sin, I might as well do it in a big way. I'm just trying to point out that what we need is research in what is effective nutrition education that brings about a permanent change in lifestyle. I have not learned how to do that.

Dr. Zemel:

Just one further comment. I think that the availability of funds to do that is so limited.

Dr. Alpert:

One quick comment - the salt taste of infants is set well before they are two years old. Unless you intervene prenatally, you are probably doomed to failure. If you can get to the pregnant mother and impart on her the importance of infant formulas rather than cow's milk, don't add salt to the food, the baby doesn't care how it tastes, and do that from infancy on and have a major component within your school system for teaching the importance of that, then two generations from now we have a chance. Until that happens, you are absolutely correct that people at our age are not going to change, no matter how much we know. Just look at how many thoracic surgeons smoke. They know better, but they are not going to change because it can't happen to them. I think it is the same attitude in the U.S. public. Hagen Daas is good because (a) it is expensive, (b) it has sex appeal and (c) you'll never get a heart attack, it's for somebody else.

Dr. Carter:

The acting head of medicine at Louisiana State University in New Orleans says that he is addicted to Hagen Daas. I want to get back to this question of coffee. Could you address Dr. Grossman's comment about coffee and hypertension - coffee and any disease.

Dr. Biaggioni:

Well, I don't know if I can do that in a very short period of time. I must agree with you that

many things we do in life will increase your blood pressure. Certainly, while I was hearing your question, my blood pressure rose more than how much yours rose when you were asking us that question. I think I agree with you that epidemiologic studies have not found any hard takers for an association between caffeine and essential hypertension, and I think our studies which are still not so extensive, draw the same conclusion that sustained caffeine intake will not adversely affect your blood pressure. I think we agree on that. The sole exception might be the patient with renovascular hypertension, but we don't know that this is the case yet.

Dr. Zemel:

I have a question, too, for you. In a recent issue of the Journal of Epidemiology, there is an article that showed an association between coffee intake and HBP, and it didn't matter whether it was caffeinated or decaffeinated, and cholesterol. I wonder if there could be some indirect association and if you would comment on that.

Dr. Biaggioni:

Right. There are some studies showing that caffeine, or coffee, will increase plasma lipids, and there is at least one study that I know of which has shown an association between caffeine intake and increased risk of myocardial infarction. I don't know about this particular study - it is hard to comment on that without knowing the methods they used, but I would say that X number of articles show an association with plasma lipids, X number of articles show that there is no association. With the limitations of epidemiological studies, there are so many factors coming into play. So many others like, maybe coffee drinkers drink their coffee while they are eating ice cream - Hagen Daas. So, those kinds of factors are so hard to control and it is hard for me to give you a straight answer, I am afraid.

Dr. Carter:

What about coffee and cancer of the pancreas?

Dr. Biaggioni:

Once more, I believe the bulk of the evidence does not support an association between those two but rather an independent association.

Dr. Howard:

Just three short questions. Despite the hair pulling and concern about whether or not we are getting the message across, clearly certain messages are getting across to the public in terms of cardiovascular disease, and there has been a striking decrease over the last decade in the incidence of cardiovascular disease. So, my first question is, has there also been a decrease in hypertension ?

The second question is, very interesting studies have been coming out about the connection between calcium intake and osteoporosis - has anybody looked in those same populations at blood pressure? And third, does anybody on the panel have any theory on how alcohol affects blood pressure?

Dr. Zemel:

I can address the second question. In a study about seven or eight years ago in central Wisconsin, Nancy Johnson and Chris Sempos were doing an osteoporosis evaluation, a long-term calcium supplementation study; they subsequently looked at blood pressure and did find a positive effect. So, I think that there is some opportunity to move across some of those studies, and I think that in the data I have seen on preeclampsia, there are some data on high calcium and low calcium intake countries in Central America that show lower preeclampsia in the high calcium intake countries. The data that I cited from Baltimore are unpublished, so I really can't say too much about them. I don't remember too much about it other than that they were very successful in calcium supplementation in a very large group of young women.

Dr. Howard:

Does anybody know if the incidence of hypertension is changing?

Dr. Grossman:

Yes, because more people are under treatment. I mean, the incidence of stroke has diminished markedly, and that is ascribed to the fact that more people are having their blood pressure checked and being treated pharmaceutically.

Dr. Alpert:
But that really addresses the prevalence of high blood pressure in the population. The question, I guess, is really the incidence - are new hypertensives occurring at the same rate? Shiriki, any ideas?

Dr. Kumanyika:
I haven't seen any incidence data.

Dr. Edozien:
I would like to explain the reason later for my question. My question is, do you have any information about the effect of low potassium diet on blood pressure in blacks?

Dr. Zemel:
We haven't done any work on low potassium diets at all. Does anyone else?

Dr. Alpert:
I know from epidemiologic studies, when I was looking at sodium, the sodium content of the black diet in the United States is not quite as high as everybody thinks it is, but the deficiency, in fact, is in potassium, and, at least in black teenagers in the south, the diet has only about half, or 60% of the sodium in teenagers.

Anonymous:
Well, 30 to 40 milliequivalents per day.

Dr. Edozien:
The reason for my question is this. I agree that the intake of potassium among blacks generally is low, but when you look at the pathology of hypertension, in blacks, they retain calcium, retain sodium, excrete potassium. And actually, potassium and zinc are the only two elements that go to feedback on the catecholamines, so that they excrete potassium as a feedback, and actually low potassium intake should be good for blacks, and so is low zinc intake, but I don't think anybody has attempted to study this.

Dr. Zemel:
I wanted to mention that we have collected blood for catecholamines in a study that we are running right now. We haven't analyzed the samples yet. So, I think that we might have some information in a year or so.

Dr. Enwonwu:
My question is directed to all the speakers. One of the purposes of this type of workshop is to identfity some areas of research priorities. Looking at the literature on the dietary interventions for hypertension, one sees a consistent pattern. Many of the dietary studies tend to monitor intake and excretions of specific nutrients to the exclusion of other potentially important factors. Such studies really tell us very little if anything about fundamental mechanisms. We also often lose sight of nutrient-nutrient interactions in the design of the studies. My question really boils down to the issue of how we design studies to evaluate how nutrients interact with one another and with the physiological systems eg hormonal, neuronal, etc, that affect blood pressure regulation?

Dr. Zemel:
I will make a comment. I think that the best of all worlds has to be a highly controlled, sophisticated study and, in our study, for example, fluoride content didn't change, because all our food was from the same lot, and we used doubly deionized distilled water, and it is the only water that was consumed. So, with the exception of phosphorus, we controlled for everything. The only thing we didn't control for was ad lib exercise, and so we were one step removed from the totally confined metabolic approaches. I think that for in vivo experiments, you need to be in a very, very sophisticated clinical setting. I mean, those experiments are very expensive to run. To run ours was probably $100,000, and we work cheap. We are very good at keeping our budget very low. I think certainly at the epidemiological level, you have multiple interactions, and at the animal level, you are not really getting at all of the interactions that could potentially occur in vivo.

Dr. Carter:
You can't eat the elephant in one bite. Speaking of preeclampsia, one of our graduate students just completed a study in Angola at the maternity hospital, and she gave one group supplements of essential fatty acids, GLA and EPA. She gave a second group a supplement of magnesium and a

third group got a placebo. Interestingly enough, they had lots of cases of preeclampsia, but they had four cases of eclampsia, all of whom survived, and all four cases were in the placebo group. The smallest rise in blood pressure occurred in the group that got the magnesium, and the incidence of edema was lowest in the group that got the essential fatty acids. And that is not even mentioning the calcium question.

Anonymous:

One of the things that caffeine has been implicated in doing is reducing the amount of blood flow to the brain, and I was just wondering, is that also enhanced after a period of abstinence, and could that be affecting the overall blood pressure by, say, stimulating neuroreceptors in CNS and affecting the rest of the body?

Dr. Biaggioni:

Actually, caffeine is known to produce, like you say, vasoconstriction of the vessels in the brain, and it is actually used to treat migraines for that reason. Heavy coffee drinkers, you may ask around of many here, will tell you that if they stop drinking coffee during the weekends, they will have a headache that is relieved by drinking coffee. This actually probably represents a withdrawal phenomena, with vaso-dilation in the brain. Now, that really doesn't mean that by drinking coffeee you will produce cerebral vasoconstriction to a dangerous degree. I don't think that there is evidence clinically for that being an important thing to worry about. Now, to your question, where is caffeine working in increasing blood pressure. That is harder to answer. Certainly, there are centers in the brain that control, to some degree, blood pressure, and caffeine, we have shown, may act in those centers. Whether it is also acting in the blood vessels elsewhere in the body by increasing peripheral vascular resistance is also an alternative. I think the problem with caffeine, as with many other substances, is that it acts in so many places that it is hard for me, especially doing in vivo studies, to pinpoint precisely where it is acting. It may be acting in more than one site.

Dr. Neser:

I have a question for Dr. Alpert. In the young adults, when we compared the medical students from Meharry and the medical students from Johns Hopkins, we found a slight reactivity excess in black medical students. But in neither study did the copressor predict hypertension.

Dr. Alpert:

Well, we have very little follow-up data. We are just collecting data and a four-year follow-up on some of these children. The one thing we have noticed is that if you look at the hyperreactors to the video game vs. the Stroup vs. the exercise vs. ambulatory, they are not the same population. The findings are somewhat overlapping, but very different groups. Some studies that Neil Schneiderman did in Miami were also very applicable. They took a group of college athletes and undergraduates who were nonathletic and gave them various tasks to do, and the individuals who were athletes were not particularly reactive to tasks that would have put your heart rate and my heart rate to 300, like putting what was supposedly a python six inches closer and closer to the subject, but mental arithmetic tasks were very difficult for the football players. So, you are really looking at task-specific reactivity and the answer probably is going to be that for hypertensive-parent, black males, so-and-so will be the best test for prediction, but for normotensive-parent, white females, another test will be what is necessary to select them out. So, as yet, we have not been able to define a test or set of tests that would be predictive, but clearly, the proof is going to be to follow individuals for twenty years and see what is the best predictor. Unfortunately, as you know, the behavioral medicine study section doesn't give twenty-five year grants as yet, but we will apply for one if asked. The problem is, in three-year bites you can hardly answer this question.

Mr. Latham:

I guess it is sort of a layman-type question. I am Sam Latham, Metropolitan Times. I have been doing a story on Dr. Holyfield, who had advanced to me a sort of controversial theory of hypertension among blacks, that blacks who were brought over here as slaves were a special type and that, in other words, the incidence of high blood pressure was increased because of ge-

netic make-up, or the genetic pool of the population that was brought over as slaves, and he claimed that that was probably more important as a cause of hypertension than diet and the other factors including environmental factors. I would like to get your comments.

Dr. Carter:

Is the panel familiar with Dr. Holyfield's work? I think he is referring to Dr. Holyfield over at Vanderbilt, who , if I remember correctly, had identified a previously undescribed hormone that might be associated with hypertension. I don't know if it ever panned out. Does anyone have any more recent information?

Dr. Carter:

Dehydroepiandrosterone, or something like that.

Dr. Alpert:

Just in a related way, at the Association of Black Cardiologists meeting last winter, an individual, unfortunately whose name I can't remember, gave a talk addressing this issue, and the explanation that he gave was that, during the evolutionary process in central Africa, the availability of sodium was so low that individuals developed the ability to save sodium and do with much less than is available in the United States. Once they were brought to the United States and were subjected to the English customs of salting things, their bodies saw an overwhelming physiologic load of sodium, and in fact their system was still geared up to preserve sodium because that is how they had evolved for the past hundred generations, that in fact they retained sodium, and their blood pressure went up. A very recent study, done in Kenya, has highlighted the same thing, with tribal groups who were drafted into the army. They took 18-year-olds who had been on a 10-15 milliequivalent sodium diet, brought them into the "westernized" society of the army. Their salt intake went up to about 180-200 milliequivalents, and within three years, an enormous number was hypertensive. So, in our westernization of society, clearly we have made people far sicker than they ever would have been had we left them alone.

Dr. Onyezili:

Does anybody have any data on blood pressure in whites during the preindustrialization period?

Dr. Alpert:

My grant didn't start then.

Dr. Neser:

The best study on that was done by John Castle, in Hilton, North Carolina, where he looked at mountaineers before Industry came in and afterwards, and there was a definite correlation with coronary heart attacks in the whites. I don't know that his paper described blood pressure specifically.

CLOSING REMARKS

C. W. Johnson, M.D.
Vice President for Academic Affairs and
Executive Vice President
Meharry Medical College

During the last two and one-half days, following Dr. Satcher's welcome address in which he described the historical mission of this college, you have been busily engaged in articulating the mission of the college at its best.

Dr. Satcher pointed out that this college has been concerned with providing access to medical education for blacks and other disadvantaged populations and, in addition to that, providing access to healthcare services for the underserved. A special part of that mission is to express concern in a positive fashion with those health problems which disproportionately affect blacks and other minority populations. Last week, AIDS was the topic of concern. This week, appropriately, the role of nutrition in hypertension in blacks is the subject of discussion.

Those of you who have come to this campus for the first time probably feel something different as you walked in, something that goes beyond the buildings. It is what I like to refer to as the spirit of this place. You have become a part of the spirit of this place as a consequence of your participation in this workshop. On behalf of the president, the board of trustees, faculty and our student body I would like to express to you my sincere appreciation for your activities in the last two and one-half days. I think perhaps Dr. Grossman might have suggested something in terms of a challenge which could be a basis for consideration at the next symposium. He has talked a little about a workshop on behavior modification during which we might get the social and behavioral scientists involved in the problems of nutrition and hypertension as well as other kinds of health issues which disproportionately affect blacks and other minorities. Thanks again and please start planning for your participation in the next nutrition workshop about a year from now.

MEHARRY MEDICAL COLLEGE
CENTER FOR NUTRITION

David Satcher, M.D., Ph.D., President, Meharry Medical College

Fred Jones, Ph.D., Vice President for Academic Affairs and Dean of Graduate Studies

Cyril O. Enwonwu, Sc.D., Ph.D., M.D.S., Director, Center for Nutrition

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